

Introduction:

Thesis on,

(A) Schistosomiasis or Bilharziasis is best defined as a group of diseases caused by several distinct species of a bisexual trematode worm which

lives chiefly in the liver and the branches of the portal system of veins. For the Doctorate in Medicine, Edinburgh University.

These diseases have, from time to time, been given different names, as for example Bilharzia by,

as cases of endemic haematuria in case of the Egyptian 1875, and Manson's disease, Okavango disease, Yangtze Lieut. Balwant Singh Bindra, M.B., Ch.B., M.R.C.P. (Edin.), D.T.M. (Liver.), I.M.S.

September 1935.

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(B) The genus Schistosoma:- In the genus Schistosoma several species have been described.

Three of these have been proved to infect man, and are therefore of considerable importance.



Introduction:- and *S. mansoni* are exclusive to man only

whereas *S. japonicum* is found both in man and domestic

(A) Schistosomiasis or Bilharziasis is best defined as a group of diseases caused by several distinct species of a bisexual trematode worm which lives chiefly in the liver and the branches of the portal system of veins. Amongst the others *S. bovis* occurs chiefly in cattle, though it has been also said to invade man in the same endemic area; this however has not been finally proved yet. *S. indica*, *S. spindalis* and *S. bomfordi* have so far been described in domesticated animals only, but it is probable that, given suitable conditions they may invade man also, and this according to Koller may explain some of the sporadic cases of valley fever, Hankow fever, Urticarial fever etc. in which have been described in India. Cases of case of the Far Eastern type, depending in some cases on the locality affected, and in others on some

These diseases have, from time to time, been given different names, as for example Bilharzia disease or endemic haematuria in case of the Egyptian conditions they may invade man also, and this according to Koller may explain some of the sporadic cases of valley fever, Hankow fever, Urticarial fever etc. in which have been described in India. Cases of case of the Far Eastern type, depending in some cases on the locality affected, and in others on some characteristic prominent clinical symptom. For the purpose of this thesis the proper generic term regarded as the natural parasites of man, causing Schistosomiasis will only be used and may be taken to cover the entire group.

S. haematobium causes the urinary type of schistosomiasis of Egypt, Africa, and the Near East.

The worm was first discovered by Bilharz in 1851, in the portal vein of a patient, and named *S. mansoni* is responsible for the intestinal form of Distoma haematobium. In 1859, Cobbold renamed it *Bilharzia* in honour of its discoverer, but as *Bilharzia* was found mainly in Central and West Africa, West Indies, and South America. The Far Weinland had already created the genus *Schistosoma* for the worm Distoma haematobium of Bilharz in 1858, Japan, and the Philippine Islands is produced by this is generally accepted by zoologists as the proper generic name.

(B) The Genus Schistosoma:- In the genus *Schistosoma* several species have been described. Three of these have been proved to infect man, and Central and North Africa, where both *S. haematobium* and *S. mansoni* are endemic and consequently infection

from both may occur in the same man.

S. haematobium and S. mansoni are exclusive to man only whereas S. japonicum is found both in man and domestic animals e.g., dogs, cats, sheep, cattle etc.

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Uptill now the first three only can be regarded as the natural parasites of man, causing definite infection with typical pathology and symptoms. S. haematobium causes the urinary type of schistosomiasis of Egypt, Africa, and the Near East.

S. mansoni is responsible for the intestinal form of schistosomiasis found mainly in Central and West Africa, West Indies, and South America. The Far Eastern type of schistosomiasis as found in China, Japan, and the Phillipine islands is produced by S. japonicum.

All three have their definite endemic areas depending on the range of limitation of the appropriate intermediary hosts. There are areas in Central and North Africa, where both S. haematobium, and S. mansoni are endemic and consequently infection

from both may occur in the same man.

(C) General Geographical distribution:- Though originally this disease was noticed in Egypt, where it has been proved to have been endemic since ancient times (by the discovery of typical eggs in mummies)⁶, and later on in Japan, and China, as work has progressed the geographical limits have been extended and fresh areas have been added where the disease has been proved to be endemic in one form or another. Today it can be safely classed as one of the most widely spread diseases in the tropics and sub-tropics.

It has been definitely proved to be endemic in large areas of Africa, Asia, and South America⁷ extending between Lat. 38° N, and Lat. 35° S.⁸ In North Africa it is common in Egypt, Morocco, Algiers and Tunis. In Central Africa it is endemic in the Sudan, Uganda, Rhodesia, and West Africa. Archibald⁹ has recently stated that 11, out of the 14 provinces in the Sudan are infected with S. haematobium, or S. mansoni. In South Africa it has been reported from the Cape, Natal, and the Transvaal. Brazil, Venezuela, and Dutch Guiana in South America are widely affected.

The Asiatic distribution of the disease may be divided into two parts. Arabia, Mesopotamia, Mauritius, and Madagascar, are affected by S. haematobium, whereas the Far East is infected widely with Schistosoma japonicum.

Distribution of S. japonicum:- The endemic area in the case of this worm appears to be restricted

to Japan, China, Formosa, and the Phillipines. In these areas most of the endemic centres are relatively small, especially those in Japan; but they are very heavily infected.

(i) In Japan the endemic centres consist mainly:-

- (a) Along the Ashida River, on the main island.
- (b) In the Katayama district of the Hiroshima, and the Okayama prefectures.
- (c) In two districts near Mt. Fuji, one to the North in the Yamanashi district, and the other on lake Ukishima at Namazu.
- (d) In the Tone River district, North East of Tokio.
- (e) On the island of Kyushu, near Kurume, on the Chikugo River.

(ii) In China the disease has been reported from mainly the central, and lower Yangtze valley, and a portion of the Siang valley in the Hunan Province. Lately fresh records have been obtained from areas in the central and lower Yangtze basin. A separate centre of infection has been located in a village near Shuichow, on the North River.¹⁰ Recently, Kastein¹¹ has reported a crop of acute cases in and around Shanghai.

(iii) In Formosa an endemic centre of Schistosomiasis has been discovered in the vicinity of Shinchiku¹², near the centre of the island where man and domestic animals have been found infected.

(iv) In the Phillipines the disease is described as being present in the Southern group of islands, Leyte, Samar, and Mindanao.^{13,14,15}

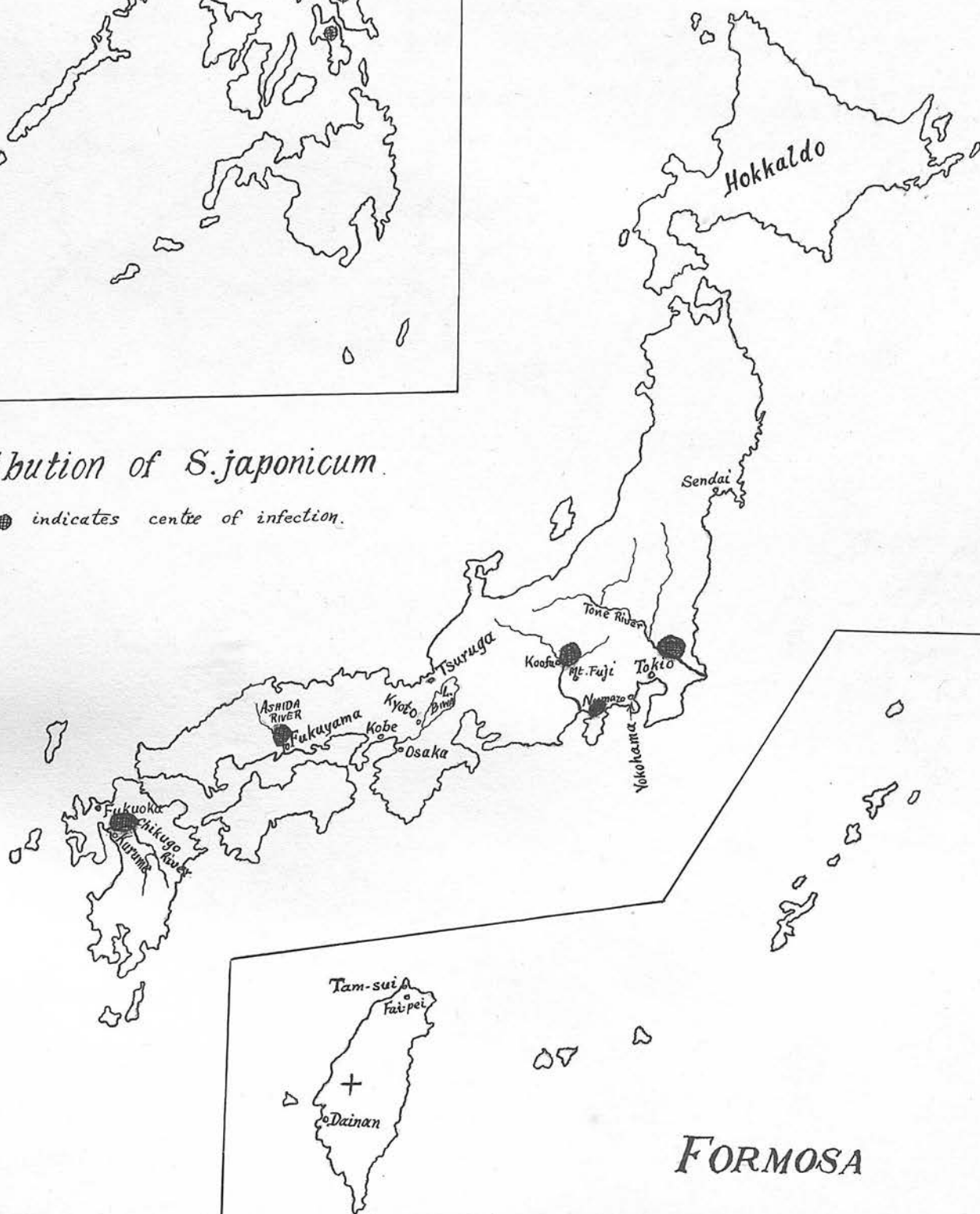
PHILIPPINE ISLANDS



JAPAN

Distribution of *S. japonicum*.

+ and ● indicates centre of infection.



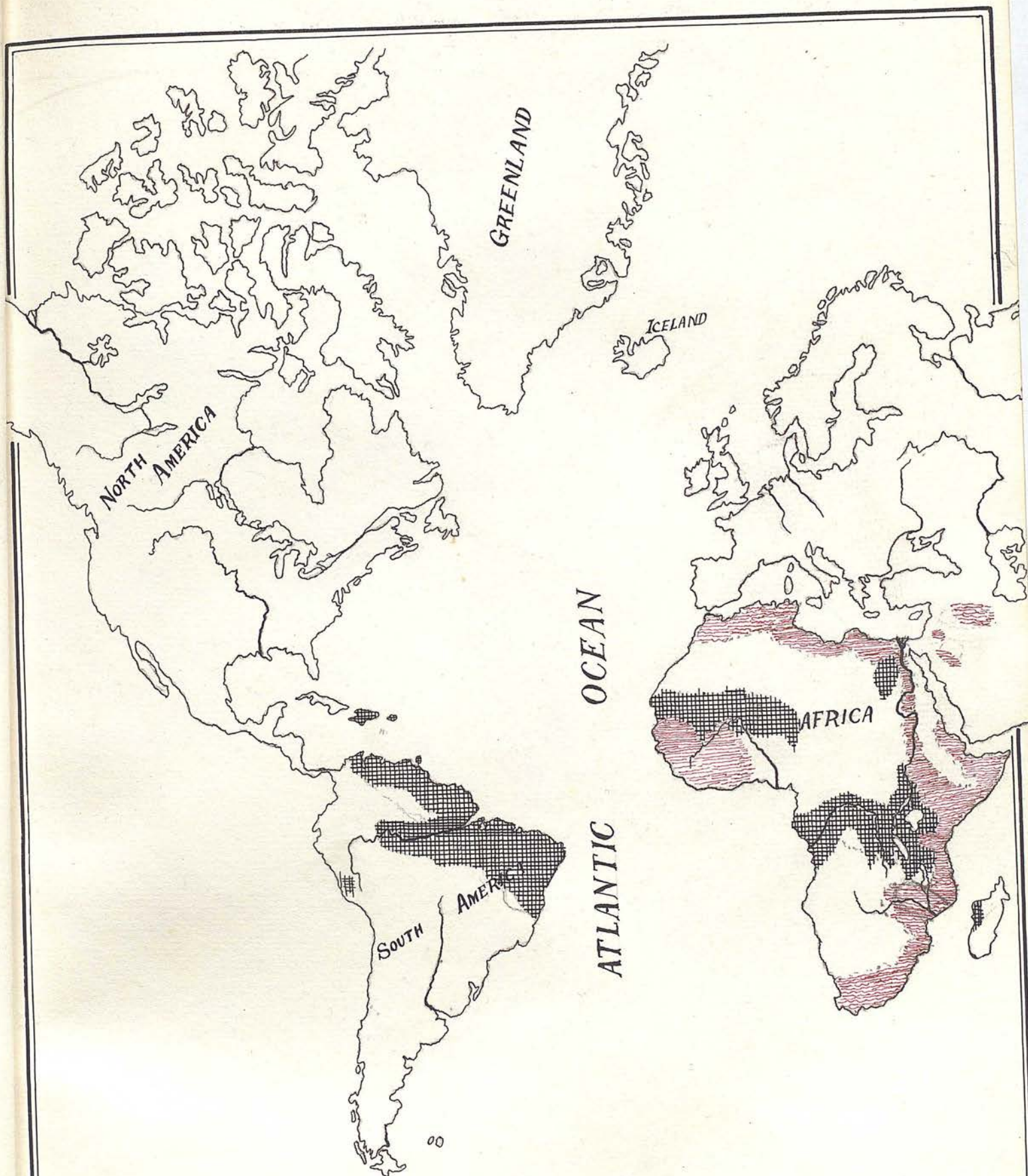
FORMOSA



Distribution of S. japonicum in

CHINA

+ indicates a centre of infection.



DISTRIBUTION OF SCHISTOSOMIASIS

■ *S. mansoni*

■ *S. hæmatobium*

Indigenous cases have also been reported from Western Australia,⁶ India, and Portugal.⁷

The distribution of the three types of human schistosomiasis is outlined in the attached maps.

(D) Recent Work:- After the original discovery of Distoma haematobium by Bilharz in 1851, progress was very slow till the first decade of the present century when the aetiology of this group of diseases was placed on a sound basis, and most points about the life history of the parasites concerned, and their mode of infection were established beyond doubt.

Amongst the prominent workers on the subject were, Katsurada, who first described S. japonicum in 1904, and later on Fujinami, Namakura, Myairi, and Suzuki, who brought out the main points in connection with the life history of the parasite. Thanks to the efforts of these workers, and others like Leiper, Christopherson, and Faust today we have a clear conception of the various aspects of this wide spread group of diseases, with resultant benefits in prophylaxis and treatment.

During the last few years the problems of diagnosis, and treatment have received a lot of attention in the various countries where the disease is endemic, and though the search for the ideal drug still continues, the position is slowly improving, and Schistosomiasis can no longer be regarded as an uncontrollable disease.

References will be made to the work of the above named, and other investigators in detail later

in the text, under the proper sections.

(E) The problem of schistosomiasis in India:-

The author's interest in the subject was aroused on seeing a case of haematuria in the King Edward Memorial Hospital, Bombay, in which the terminal spined eggs of S. haematobium were seen in large numbers. This man however, came from Mesopotamia, and had also visited Egypt.

On further investigation it was found that several similar cases had been seen here from time to time but one could always trace the origin of the disease to the patient having visited some endemic area.

This gave rise to the problem as to whether schistosomiasis could spread in India. On first thought it would appear that this country should afford ideal opportunities for the spread of this disease, on account of the lack of proper sanitary arrangements over thousands of miles of its rural area. The habits of people living in the country also should suit the spread of this disease. In so many villages the same ponds are used for the disposal of excreta, and washing and bathing. Most of these ponds and streams are heavily infested with snails, closely allied to those concerned in the development of the larvae of these worms.

The fact that so far the country appears to be free from this disease may possibly be due to:-

(1) The infected people who come to this country from the endemic areas usually come for

business purposes and stay in big towns where the sanitary arrangements are quite satisfactory, both in connection with the disposal of excreta as well as the purification of the water used for drinking and bathing.

(2) Large numbers of infected cases are amongst the soldiers coming from Egypt, Mesopotamia etc., and here again they live in cantonments where there is strict discipline and control regarding the disposal of their excreta.

(3) Another possibility is that the snails found in India, though they appear to be allied to the ones found in the endemic areas, are not suitable for the development of the schistosome larvae. It has however been proved that several species of snails can serve as intermediary hosts for the same worm, e.g. in Venezuela S. mansoni larvae can develop in Planorbis guadalupenses¹⁸ whereas in Brazil Planorbis oliveacicus serves as the intermediary host.¹⁹

Discussing the possibility of the Indian snails serving as intermediary hosts for schistosome larvae, Sewell²⁰ has remarked that the genus Bullinus is almost unknown in India, nor has Hypsobia (Katayama) been so far described in this country, and the other snails, e.g. the various species of the genus Planorbis are already so heavily infected with other cercariae that a new comer has practically no chance.

One important point which has to be ascertained at this stage is whether the disease

already exists in India. On going over the records it appears that though several cases of this disease have been described^{21,22,23} from time to time, there are only about five which could be said to be definitely indigenous. The first of these was described by Dr. A. Powell^{24,25} in 1903, in a syce from Ahmednagar, who had never been out of India. An interesting fact about this case is that Ahmednagar was a camp for Boer prisoners during the South African War many of whom were infected with these worms. The second case was recorded by Sewell²⁶ in a British soldier in Mian Mir who had never been to South Africa or Egypt. The third case was described by Christophers, and Stephens²⁷ in a native of Madras in whose urine they found the typical terminal-spined eggs of S. haematobium, and some peculiar spindle shaped eggs. The fourth case was reported by Major Hooton²⁸ in a Parsi girl aged five years who was suffering from haematuria, and passing terminal spined eggs in the urine. In 1922, Harkness²⁹ found ova of S. haematobium in the urine of a man in London who had lived in India for four years and had visited no other country.

Milton³⁰, while discussing the possibility of schistosomiasis in India remarked that the two cases reported by Wardrop²² in 1906, were most probably indigenous, because they came straight from England to India and developed schistosomiasis within 6 months.

The fact that inspite of such a large number of keen observers having been working in India, only

five or six cases of an apparently indigenous nature have been described would go to prove that the disease does not naturally occur in this country.

In the case of S. mansoni, however, there is so little in the shape of signs and symptoms in the early case, and later on when the disease is fully developed it resembles chronic dysentery so closely that it would require a most careful and systematic examination of a large number of suspicious cases before a fair opinion regarding the presence or absence of the disease in the country could be given. Morawitz examined the stools of several apparently healthy cases in Porto Rico, before he was able to demonstrate the typical lateral-spined ova, and establish the existence of the disease in that country.

Similarly in the case of S. japonicum the prominent symptoms like fever (of a chronic type), diarrhoea, enlarged liver and spleen, ascites, anaemia etc., resemble diseases like malaria, and kala-azar so closely that it is quite conceivable that such cases might have been missed in the past. Here again careful routine examination of stools for ova of this, or some other similar parasite may help to clear up the position.

As regards schistosomiasis in animals in India, Soparker³¹ examined several hundred animals slaughtered in Bombay and found quite a number of sheep and buffaloes infected with a parasite closely allied to S. indicum. In the case of the oxen he found that they

were more often infected with S.spindalis. S.bomfordi³² and S.bovis have also been recorded in the animals in this country. According to Montgomery, schistosomiasis is an established disease in horses, donkeys, cattle, sheep, etc. in Northern India.

Whether these parasites are, and will remain exclusive to animals only is difficult to say at present, but when one compares the position with S.japonicum, where the same parasite can affect both man and animals, it does not seem unlikely that this disease (if it is not already present in the human beings in this country) may spread to man and assume considerable economic importance. S.bovis has already been said to be able to infect man², and similarly Christopher's case with spindle shaped ova in the urine may have been due to infection with a parasite usually found in the animals. Cawston⁴ recovered some ova resembling those of S.spindalis from the urine of a Zululand school boy. In 1926, Annie Porter⁵ worked out the life history of a variety of S.spindalis (Montgomery) recovered from two cases of human infestation in South Africa.

Chandler³³ has described a peculiar type of schistosome egg in two cases, found in fresh human stools. One cannot attach too much importance to these, because in both cases the stools were collected from fields, and though they were obviously human no further information regarding the infected person is available. One case was from a village on

near Krishanagar in Bengal, and the other one was in Nepal near Kalipong. In both these cases he found typical schistosome eggs, yellowish brown in colour, measuring about 95 μ by 42 μ with a sub-terminal spine about 8 μ in length. He also noticed the outline of a miracidium in one of them. As these eggs differed morphologically from all the other species so far described, he created a new species for them giving it the name S. incognitum. These findings have not been confirmed by any other observer.

(F) Economic importance of schistosomiasis in India:- The economic importance of the incidence, and control of a disease like schistosomiasis can hardly be over-estimated; especially in a country like in India, where a vast majority depends solely on agriculture. According to the latest census³⁴ 67% of India's workers live on agriculture. At an average there are about three to four dependants on every working man in the rural areas, and consequently the illness of one man may deprive so many of their daily bread. At the same time a chronic debilitating disease like schistosomiasis, if allowed to spread may to say nothing of the suffering of the affected, affect the agricultural produce of the country to a very large extent, and thereby hamper the progress of the country.

It is needless to say that if this disease once takes a hold in this country, it is going to be a very difficult problem to get it under control, on accommodation for about 400 in-patients.

account of the extreme degree of ignorance and lack of education amongst the rural populace.

When one remembers that according to comparatively recent estimates, there are over ten million sufferers from this disease in China, and about six million in Egypt, one gets an idea of the importance it can attain in an affected country. In a village called ^{2c} Marg in Egypt, Leiper³⁵ found that 49 out of 54 school children examined were infected. Hall³⁶ examined the school children in Iraq, and found that 63% in Government schools, and 48% in American schools were infected with schistosomiasis.

Taking these points into consideration it is obvious that a very sharp outlook must be kept for any suspicious cases, and every available described case should be carefully followed up to its probable source of infection. This vigilance will have to be kept until such time when the endemicity of the disease, or even the possibility of its becoming endemic in this country can be definitely excluded.

(G) Purpose and scope of thesis:- While working as the medical registrar in the King Edward VII Memorial Hospital in Bombay, during the last year, the writer had the opportunity of studying this problem from various points of view as affecting this locality.

The hospital is one of the largest and best equipped in the country, the average daily number of new out-patients attending being about 250, with accomodation for about 400 in-patients.

A large proportion of the patients are mill hands (the hospital being situated in the mill area), but a good few lower class working people from the city and fishermen and agriculturists from the suburbs and the neighbouring villages also attend regularly.

Practical work was carried out mainly on the following lines:-

(1) A careful examination of the stools for the presence of schistosome ova was carried out in a certain number of patients suffering from obscure anaemias and dysentery.

(2) Side by side with the above, total and differential leucocytic counts were carried out in these cases to find out if any of them showed an increase in the percentage of eosinophils.

(3) A large number of snails were collected from several fresh-water tanks and ponds in the vicinity of Bombay, and these were examined for possible infection with schistosome larvae; the cercariae obtained from these snails were carefully examined.

(4) Some cases from the M.E.M. Hospital, and a few fishermen from a small village in the vicinity of Bombay, (who spend several hours daily in fresh water where a large number of snails were found) were examined serologically with an antigen prepared from livers of *Planorbis* snails infected with *S. spindalis*, for possible infection with schistosome worms.

Side by side with the above work a thorough study of *S. japonicum* was undertaken because of the following reasons:-

(a) As already stated *S. japonicum* infects both men and animals in the same locality, therefore one has to bear in mind the possibility of animal schistosomiasis (which is definitely known to be quite common in this country) spreading to man.

(b) Cullen³⁷ has recorded 9 cases of schistosomiasis *japonicum* in Burma. Because of the proximity of this country to China and Japan, and the increasing amount of traffic between these countries there is a greater danger of the spread of *S. japonicum* in this country than any of the others.

(c) Bhalerao³⁸ has remarked that the six male schistosome worms obtained by Maplestone from the intestine of a pig in Calcutta were indentified as *S. japonicum*. Sewell³⁹ found cercariae morphologically indistinguishable from those of *S. japonicum* in *Indo-planorbis exustus*, and *Limnea amygdalum* snails. It would appear from the above that *S. japonicum* or some very closely allied species is already present around Calcutta.

(d) Milton⁴⁰ reported in 1924, that *S. japonicum* was probably present on the West coast of India, and stated ".....the fact that India is not only threatened but already infected on the Eastern border is a matter affording grave food for reflection on the part of the authorities concerned."

In the present thesis it is proposed to give a resume of our knowledge of S.japonicum, (comparing it with S.haematobium, and S.mansoni in the more important points) and an account of the author's finding in the practical work carried out in Bombay, and their significance.

Finally the position of this country with regard to this disease, and the possibility of its spread will be summarised, and the practical methods that may have to be employed in the control of a possible out-break will be discussed.

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Historical outline: - (iliated embryo), as it came out

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Urinary schistosomiasis has been known in directly by penetrating intact skin. According to Egypt, since the Pharonic times as proved by the discovery of calcified remains of typical schistosome ova by Sir A. Ruffer¹, in the mummies of the twentieth dynasty (1250-1000 B.C.); but the cause of this wide spread disease was obscure till the year 1851, when Theodor Bilharz² of the Medical School in Cairo discovered a peculiar bisexual trematode in the mesenteric veins of a patient at the Kasr-el-Aini Hospital. The same worker, at a later date³, associated the presence of this worm in the

veins with the symptoms of haematuria, and the passage of typical terminal-spined eggs in the urine.

Some time later, in 1864, John Harley⁴ found similar worms in patients who had suffered from haematuria in the Cape Colony, and Natal.

On analogy with the other known trematodes it was realised that the parasite probably had an intermediate host, and several observers like Cobbold⁵, Sonsino⁶, and Loos⁷ unsuccessfully tried to find the invertebrate host during the period 1870-95.

Loos was the first to describe the anatomical structure of this worm in 1895, but it appears that this description had to be modified later because he had included some of the characters of S. monsoni, particularly in his description of the testes and the gut. On being unsuccessful in finding the intermediate host, he formulated the theory that the

the author of this suggestion.

miracidium (or the ciliated embryo), as it came out of the egg, was capable of infecting the adult host directly by penetrating intact skin. According to him the only known host of S. haematobium was man.

In case of S. mansoni, it appears that the existence of lateral-spined ova was recognised by Griesinger and Bilharz, but the difference in the position of the spine in the two types of ova was first suggested by Sonsino⁸. He first thought that the lateral-spined ova belonged to a different species, but later on he stated that these two kinds of ova gave rise to male and female embryos respectively, proving beyond doubt the important

Manson⁹, in 1903, on finding lateral-spined ova in the faeces of a patient from Antigua, West Indies, who had never been to Egypt compared the position with (the then newly described) S. japonicum, and suggested the possibility of the existence of a third species. He based this suggestion mainly on geographical grounds, and the absence of urinary symptoms in the cases in South America, Congo Free State, West Indies, Porto Rico etc., where lateral-spined ova were frequently seen in the faeces.

Samson¹⁰ elaborated these points in 1907, and described the distinct geographical distribution, pathology, and the uniformity of structure of the egg, and named the species S. mansoni in honour of the author of this suggestion.

Holcomb¹, in the West Indies in 1907, and da Silva² in Brazil in 1909, described the anatomy of the adult S. mansoni, bringing out the main points of difference as compared with S. haematobium with special reference to the tuberculation of the cuticle, and the number of testes.

In spite of these descriptions, Loos³ severely criticized Sambon's views, and denied the existence of S. mansoni.

This controversy was not finally settled till 1916, when Leiper⁴, as a member of a special mission sent out by the War Office to investigate the problem, succeeded in proving beyond doubt the important points in the life histories of these worms. He was able to work out the complete life history of both the species, and define the snails which could act as intermediate hosts in each case. He pointed out the minute differences between the cercariae, as derived from Bullinus (sinistral and spiral fresh water) snails in the case of S. haematobium, and Planorbis (flat fresh water) snails in the case of S. mansoni. He was also able to infect animals (rats and monkeys) with these cercariae, and trace the infection to the development of the adult males and females in each case. At the same time he brought out some of the important points in the prophylaxis, and the prevention of spread of this disease as applied to Egypt.

Side by side with the work in Egypt, thees to problem of schistosomiasis had been attractingout considerable attention in other parts of the world. In India, Montgomery¹⁵ described three more species, namely S. indicum, S. spindalis, and S. bomfordi in horses, sheep, cattle, and other domestic animals, in 1906. under which the disease was then known),

and was But real epoch making work was carried out in Japan, and most of the important points in the life history of these worms were brought out for the first time by the discoveries made in that country. The history of S. japonicum may be briefly outlined as follows:- of the adult worm as being in the

The earliest recorded account of this disease in Japan is that of Fuji,¹⁶ who first described the disease in the Katayama district in 1847. cribed it in Jan

The work was followed up by Balez,¹⁷ in 1883, who described the endemic district of Okayama, and worked out the infective incidence of this disease in some villages. He also described most of the cases clinical features of the disease e.g., enlargement of the liver and spleen, diarrhoea, anaemia, fever, ascites etc. but was wrong in attributing these to infection with a liver fluke (*Clonorchis sinensis*).

Several observers e.g. Yamagiva¹⁸ in 1890, and Kurimoto¹⁹ in 1893, found eggs of an unknown parasite in various organs of infected people dying of this disease. Kasai²⁰ was the first one to find the typical eggs in the faeces in 1903. laboratory

The credit of describing S. japonicum goes to Katsurada²¹, who brought out most of the facts about this worm, including the morphology of the eggs, and the adult worms, and contrasted these with S. haematobium. He found the eggs in the faeces of several patients suffering from Katayama disease (the name under which the disease was then known), and was able to find the adult worms in the portal system of cats. He named the species S. japonicum.

In the same year Tsuchia²² found the parasite in dogs, cats, and men. In 1907, Fujinami²³ worked out the pathological anatomy of the disease, and described the habitat of the adult worm as being in the portal system of veins.

Catto,^{24,25} independently found the worm on an autopsy in a Chinese from Fukien, and described it in January 1905, he was evidently mistaken in stating that the adult worms were found both in the mesenteric arteries and veins.

Following upon these discoveries several cases of infection with this parasite were reported from various centres in the Yangtze valley in China.

Further progress was made in 1909, when Fujinami, and Namakura²⁶ carried out extensive scientifically controlled experiments in the Katayama district. By exposing experimental animals (cats, dogs, and calves) to infected rice field water, they were able to prove that the infection took place through the skin. They found that laboratory

animals e.g. guinea pigs, and mice were also susceptible to infection with this worm, and were able to produce the various stages of the adult worms by allowing continuous infection to take place in the same animal.

Matsura²⁷ allowed himself to be infected by immersing his legs in infected water and proved that infection in man also took place through intact skin.

Miyagawa,^{28,29} while working on the course taken by the worm in the adult host, in 1912-13, found that after passing through the skin the worm could travel either through the veins or through the lymph channels. He also concluded that the form of the parasite which affected the adult host was (being smaller and with shorter cilia) different from the one coming out of the hatched egg, and resulted after change of generation in an intermediate host. (1921).³⁵ The part played by the snail in the life history of the worm (including a description of the species of snails concerned) was brought out by Miyairi, and Suzuki³⁰ in 1913-14. They were able to infect snails with hatched miracidia obtained from the eggs in an infected calf's dung, and study the further development of these miracidia. They also succeeded in infecting experimental animals with cercariae obtained from these snails. This completed the life history of the parasite.

Later on Narabayashi³¹ in 1916, and Sueyasu³² in 1920 (working with serial sections of experimentally

infected mice) concentrated on working out the course taken by the parasite in the adult host after passing through the skin to reach the portal veins, but the position on these points is not quite clear yet.

During their visit to China, and Japan in 1915, Leiper, and Atkinson³³ repeated and confirmed the experiments of the Japanese workers. They however, were not able to find the intermediate host in the endemic area they visited.

The finer points in connection with the S. japonicum cercaria were not brought out till the publication of Cort's account in 1919.³⁴ He studied the cercariae obtained from Japanese snails which had been shipped in dry earth. He has also added materially to our knowledge of the development of the worm in the adult host by studying young worms in the tissues of experimentally infected mice, (1921).³⁵

As regards the prophylaxis in connection with S. japonicum Miyagawa³⁶ tested the resistance of schistosome eggs to various chemicals, in 1916, and found lime to be the cheapest, as well as the most effective. Fujinami, and Sueyasu³⁷ tried the effect of the various calcium salts on the larvae, and snails, and found calcium oxide to be most effective.

Work on the treatment of the infected individuals progressed at a much slower rate.

Work on the pathology, clinical aspects, and treatment of the disease will be referred to in the proper sections.

Hutchison³⁸ first noted the efficacy of emetine in the treatment of S. japonicum infection in 1913. Later on other workers like Diamantes,³⁹ Bonne,⁴⁰ and Erian⁴¹ found it effective against the Egyptian type of the disease also. In 1912, Miyagawa⁴² remarked on the usefulness of quinine hydrochloride in the treatment of schistosomiasis in Japan. VI 1856, pp. 49-65.

McDonagh⁴³ tried tartar emetic in the treatment of schistosomiasis during the Boer war, but his results were not published till 1915.

Christopherson,⁴⁴ while working at the Khartoum hospital, in 1918, was the first one to place the treatment of schistosomiasis on a sound footing. He claimed that in Antimony we have a cure for both S. mansoni, and S. haematobium, as well as a reliable prophylactic. Cawston⁴⁵ and Libby⁴⁶ tried it and found it efficacious in the Japanese type of the disease also.

Another important advance, in our knowledge regarding schistosomiasis was marked by the elaboration of a Bordet-Gengou Complement fixation test by Fairley⁴⁷ in 1919. By means of this test (which was confirmed by Murray⁴⁸ in 1920) infection can be detected in the early stages of the disease before the appearance of ova in the dejecta.

During 1921, and 1922, cases of infection in man with S. bovis were described by Cawston in Natal, and Reynaud, and Leger⁵⁰ in the Congo.

Work on the pathology, clinical aspects and treatment of the disease will be referred to in the proper sections.

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- (a) The adult *S. japonicum*: - These worms are found principally in the vena porta and the splenic, though they have also been found in the splenic, and the superior mesenteric veins.
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Aetiology and Pathogenesis:-

(a) The adult parasites:-

(i) S. japonicum:- These worms are found principally in the veins of the large intestine, though they have also been found in the splenic, gastric, and the superior mesenteric veins.

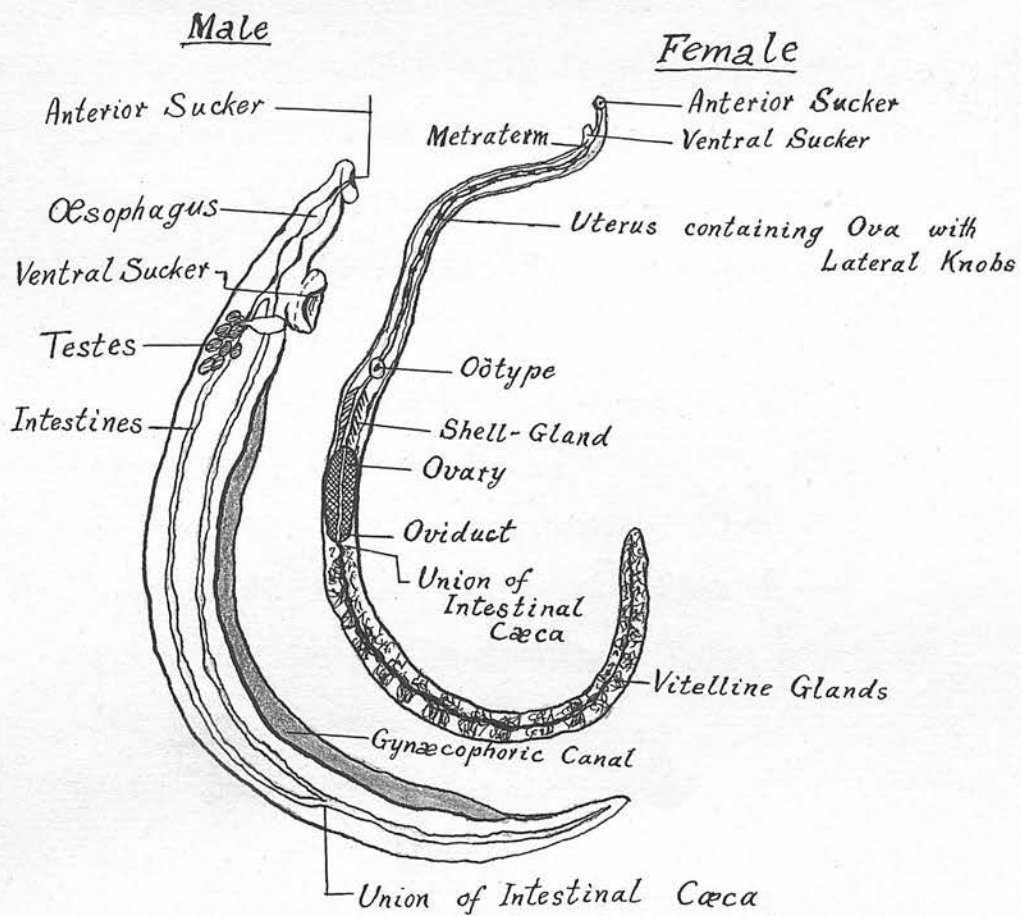
The male is a whitish, flat, leaf like worm broader at the centre than the extremities. The anterior end is narrow, and bears two prominent suckers close to each other. The posterior end is bluntly rounded. At an average this worm is about 9 mm. in length by 5-1 mm. in breadth. In life the two margins are folded up on each other ventrally, forming the gynaecophoric canal in which the female is partially enclosed; this gives the worm a cylindrical appearance.

The cuticle is smooth except on the ventral surface, where a few spines are found.

According to Loos¹, the muscular system of this worm is very highly developed, and makes up in part for the absence of cuticular excrescences in aiding the worm to maintain its position in the blood stream.

Out of the two suckers, the oral sucker is situated at the pointed anterior end of the worm; it possesses several series of powerful muscles. The ventral sucker being stouter in build and distinctly pedunculated, has a funnel shaped appearance.

The alimentary system commences at the mouth in the oral sucker, and leads into a short straight



SCHISTOSOMA JAPONICUM

oesophagus, which is provided with two lateral bulbs. The oesophagus bifurcates into two lateral intestinal caeca at the level of the ventral sucker. These caeca pass backwards in the lateral borders of the parasite running parallel to each other, and reunite to form a single median tube. This united gut ends near the posterior extremity of the worm, and occupies about $\frac{1}{4}$ of the total body length in this species. The excretory system consists of two longitudinal canals which run along the entire length of the worm, and open into the excretory pore situated posteriorly and dorsally. The reproductive system consists of 6-8 elliptically shaped testes situated dorsally in the (acetabulum) ventral sucker. The vasa efferentia join together to form a common duct, which opens slightly posterior to the acetabulum, where there is a large seminal vesicle. The nervous system is represented by an oesophageal ganglion from which two longitudinal nerve cords proceed towards the posterior end of the body. These cords intercommunicate at different levels by means of lateral branches. The male is considerably larger. The female is cylindrical and considerably longer than the male, being about 12 mm. in length, and 3-4 mm. in breadth. When the worms are paired the central part of its body is enclosed in the gynaecophoric canal of the male, while the anterior and posterior parts remain free.

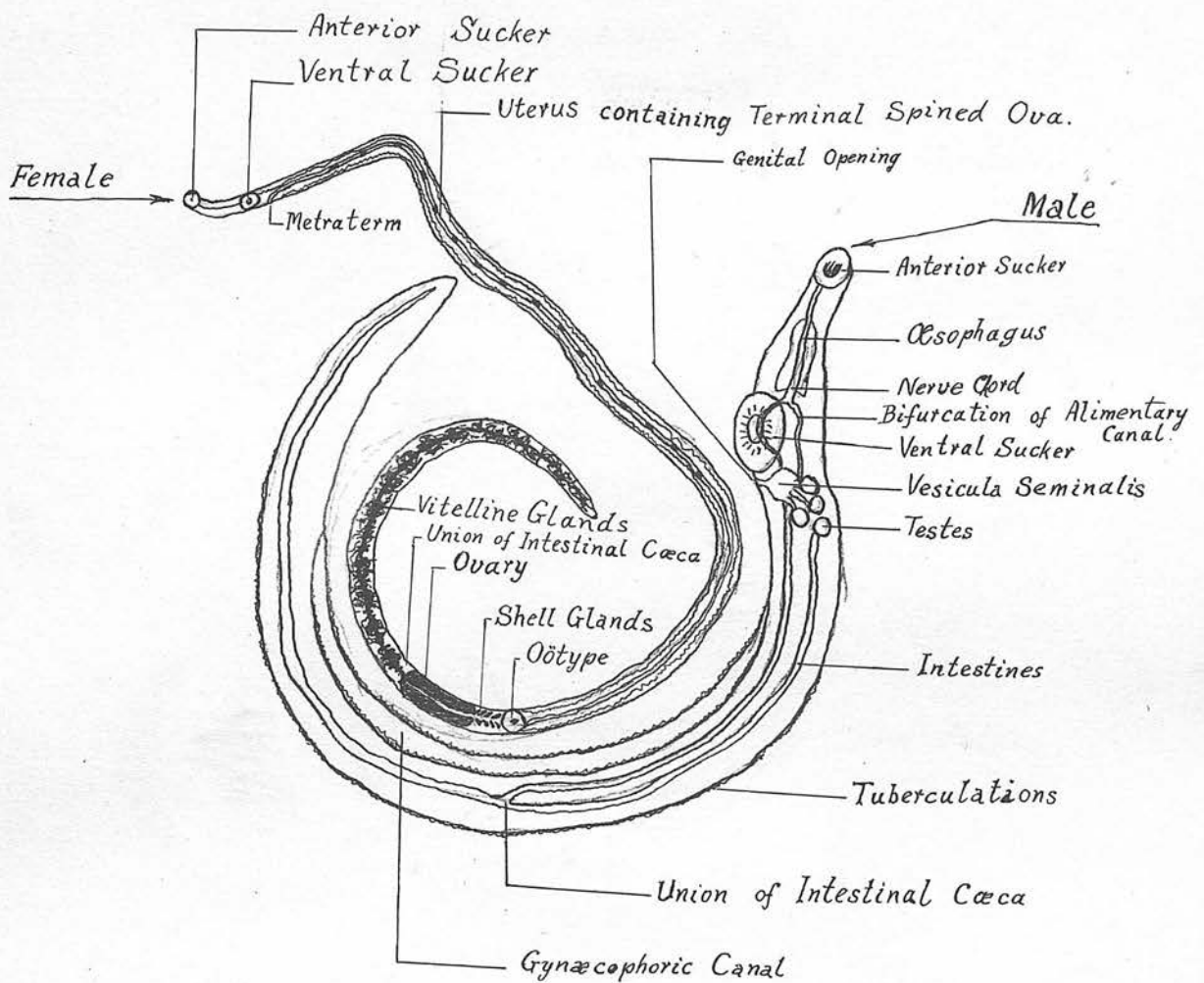
In general structure the female is similar to the male, except for the fact that the suckers are much smaller.

The genital system consists of a large ovary situated in the middle of the body, just in front of the point of union of the intestinal caeca. The oviduct arises from the posterior pole of the ovary, and as it passes forwards it is joined by the vitelline duct. The shell-gland opens into the oviduct as it emerges from the anterior pole of the ovary to become the uterus. The uterus occupies the anterior part of the body extending as far as the genital pore, situated just behind the ventral sucker. It may contain 50-200 ripe eggs. The posterior part of the body is filled up with well developed yolk glands.

(ii) S. haematobium:- In addition to the mesenteric branches of the portal veins these parasites are found in the vesico-prostatic, the public, and the uterine plexuses. Occasionally they have been found in the venacava, and even the pulmonary vessels.

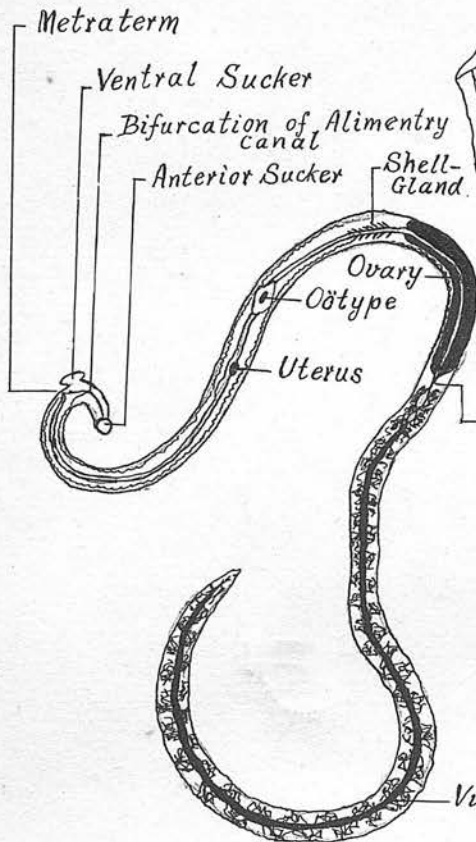
In general structure and appearance they are similar to S. japonicum. The male is considerably larger than S. japonicum, being 11-15 mm. in length by 1 mm. in breadth. Its cuticle is finely tuberculated. The genital system consists of four large irregularly rounded testes.

The oesophagus is devoid of bulbs, and the intestinal caeca reunite near the posterior end of

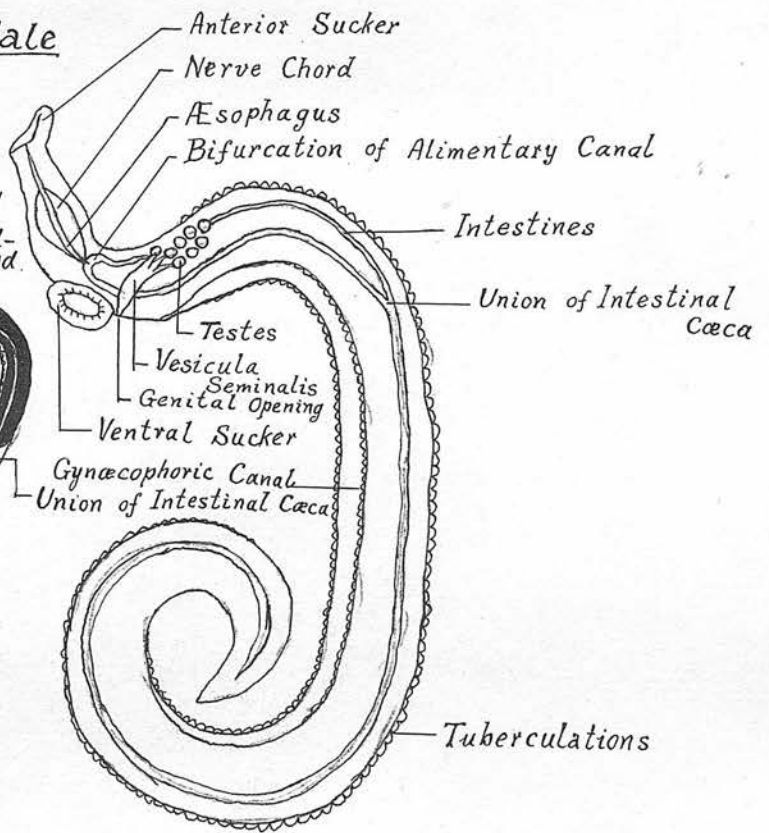


SCHISTOSOMA HÆMATOBIUM

Female



Male



SCHISTOSOMA MANSONI

the worm, forming a short united gut.

The female is longer and more filiform, being 20 mm. in length by .25 mm. in breadth. Its body is smooth except towards the posterior end and on the suckers, where papillae abound. The ovary is situated near the posterior end. The uterus is very long and may contain several hundred terminal-spined ova.

(iii) S. mansonii:- These are more commonly found in the veins of the intestinal tract, especially in the haemorrhoidal plexus, and the inferior mesenteric vein. They are also found in the branches of the portal vein in the liver.

In general structure these worms are similar to S. haematobium. The size is slightly smaller in both sexes; the male being 10 by 1-2 mm, and the female being 15 by .16 mm.

In the male the skin is very grossly tuberculated, and it possesses 8-9 small testes.

In both sexes the oesophagus bifurcates at the level of the ventral sucker, but the reunion takes place in the anterior half of the body. In this species the united gut occupies approximately the posterior $\frac{2}{3}$ of the total body length.

In the female the ovary lies just in front of the union of the intestinal caeca, and in consequence the uterus is very short. It contains 1-3 laterally spined eggs. The entire length of the body behind the ovary is filled up with yolk glands. stout, and very definite spine.

(b) The Ova:-

(i) S. japonicum:- These ova show a considerable degree of variation in shape and size, depending on the stage of growth and development.

The fertilized egg, as seen in the uterus of the adult female worm is ovoid in shape, and measures at an average about 70 μ in length by 50 μ in breadth. It is hyaline in appearance, and there is a small cup like depression on the side near the anterior end which bears a small rudimentary spine.

The exact size of the mature egg, as seen in the stools depends mainly on the time interval between its oviposition in the intestinal wall, and the time when it is examined. The average fully matured egg measures about 85-90 μ in length by 65-70 μ in breadth. There appears to be a great variation in the exact figures recorded by various observers; this according to Faust and Meleney² may be due to the degree of maturity of the eggs measured.

Some observers e.g., Castellani and Chalmers³ have described a cap like thickening on the side of the egg opposite to the rudimentary spine. These eggs are voided in the stools of the definitive host, and ciliated miracidia hatch out from them.

(ii) S. haematobium:- These ova are much larger in size as compared with those of S. japonicum. They are usually oval or spindle shaped, and each egg at an average measures about 160 μ in length by 60 μ in breadth. At one end of the egg there is a short, stout, and very definite spine.

HUMAN BILHARZIOSIS. DIFFERENT EGGS.



S. HAEMATOBIIUM
150 x 60 μ



S. MANSONI
147 x 67 μ



S. JAPONICUM.
83.5 x 62.5 μ .



CHRISTOPHAR'S CASE.
205.2 x 53.2 μ .

ANIMAL BILHARZIOSIS. DIFFERENT EGGS.



S. INDICUM.
130 x 70 μ .



S. BOMFORDI.
170 x 80 μ .



S. BOVIS.
170 x 45 μ .



S. SPENDALIS.
380 x 70 μ .

They are voided in the urine, and rarely in the faeces of the vertebrate host. The egg hatches by rupture of the shell, and a ciliated miracidium is liberated.

(iii) S. mansoni:- The eggs in this species are more bluntly oval than those of S. haematobium. They measure about 150 in length by 56 in breadth at an average.

These eggs are usually passed in the faeces, and hatch out a ciliated miracidium.

(c) The free embryo or miracidium:-

(i) S. japonicum:- During life this is cylindrical in shape, being about three times as long as it is broad. It takes on very active movement as soon as it escapes from the egg, and its structure can only be studied by examining fixed specimens.

Considerable variations have been noticed in its shape and size. In the earlier stages it is cylindrical, but later on it becomes more flat from side to side. It averages about 95-100 μ in length by 35-40 μ in breadth; in the later stages the breadth may increase to 50 μ or even more.

The movement takes place by means of cilia, which cover the entire body except for a small area at the anterior end. These are mainly of two types. There is an anterior group of densely arranged fine hair-like cilia extending as far laterally as the openings of the lateral glands. As a contrast to the above are those in the posterior group, which

are much stouter, and are more widely spaced.

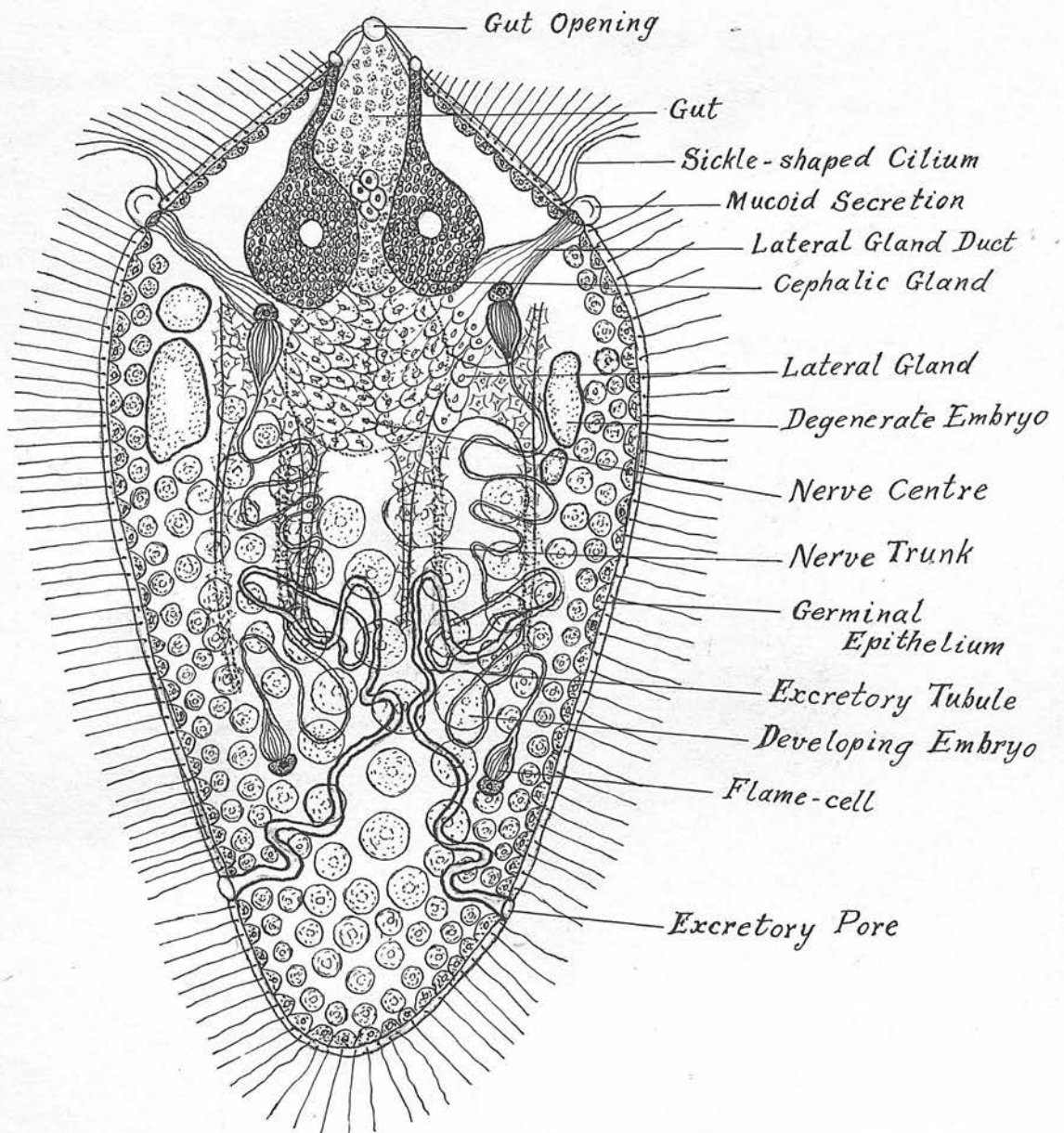
The alimentary system, which does not function at all in this short lived organism, consists of an oral opening at the anterior end leading into a small sack like gut which contains four prominent nuclei embedded in its substance.

Lateral to the gut there are two prominent pear shaped cephalic glands, each containing a central nucleus, and packed with fine eosinophil granules. These glands open anteriorly, one on either side of the oral opening.

Behind the cephalic glands is a mass of fibre like structures which have been described as the lateral glands, opening one on each side. Faust and Meleny have obtained a mucoid secretion from these glands.

The nervous system consists of a mass of round nucleated cells, situated behind the lateral glands. On careful examination a few band like structures can be seen passing anteriorly, as well as in the posterior direction from the central mass.

The excretory function is carried out through four large flame cells, two draining the anterior part of the organism, and two the posterior part. The tubules from the two flame cells on each side unite to form a collecting tubule, which opens in the posterior third of the body, by means of an excretory pore.



MIRACIDIUM OF S. JAPONICUM

posterior. The bulk of the embryo is occupied by a large number of germ cells, which have arisen from the germinal epithelium lining the entire body cavity. Some of the germ cells degenerate and form structureless masses. Adapted for motility and penetration.

(ii) S. haematobium:- Structurally this is similar to the embryo of S. japonicum, but it is much bigger in size. than the body, and is characteristic-

ally of (iii) S. mansoni:- The embryo of this species is of a medium size as compared with the other two. According to Cort⁴, in this embryo the cephalic glands are much larger in proportion to the body length.

prominent suckers. The anterior one is greatly

(d) The cercariae:-

developed in this species, occupying almost the anterior third of the body. And its rim is provided with some minute papillae. The ventral sucker is the intermediate host on completion of development comparatively much smaller in size, and lies in the posterior third of the body. Therein and are ready to infect the adult host.

In this stage it is possible to distinguish the species of trematodes which can infect man from the others. Leiper⁵ has pointed out the following four important characteristics of the cercariae which can produce human schistosomiasis:-

1. They have forked tails.
2. They do not possess a pharynx.
3. They have no eye spots. (These are minute collections of dark pigment, located anteriorly one on either side.)

The excretory system consists of two pairs of flame cells for the body, and one pair for the tail.

4. They have two sets of glands communicating with the mouth, and lying on both sides of the capillary canals from these flame cells join to form

posterior end of the body.

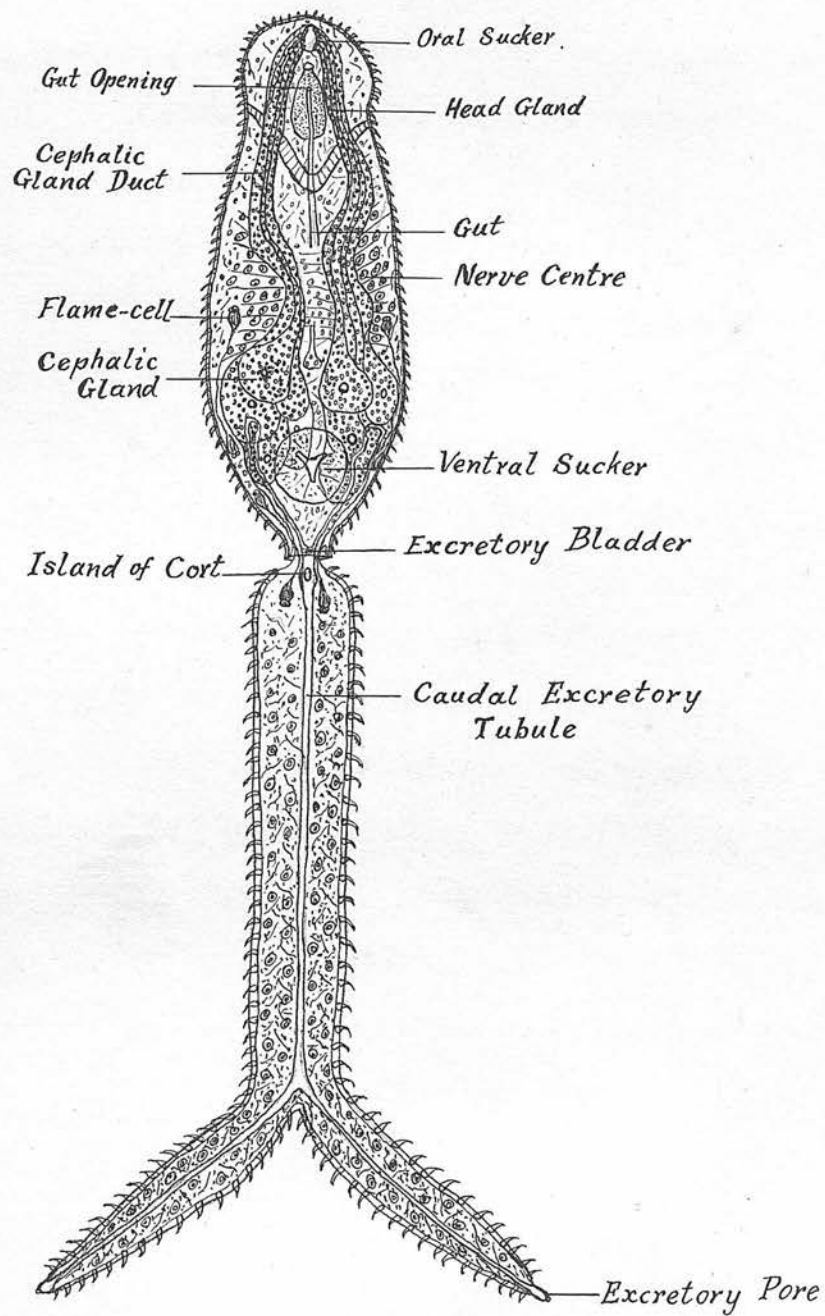
(i) The cercaria of S. japonicum:- This is a more highly developed structure than the miracidium, and possesses a body and an elongated tail. It is specially adapted for motility and penetration.

The body is oval in shape, and measures about 120 in length by 40-50 in breadth. The tail is slightly longer than the body, and is characteristically bifid at the end, each of the furci measuring 40-50 in length.

The outer cuticle of the body and tail is covered by strong reversed spines. There are two prominent suckers. The anterior one is greatly developed in this species, occupying almost the anterior third of the body, and its rim is provided with some minute papillae. The ventral sucker is comparatively much smaller in size, and lies in the posterior third of the body.

The digestive system consists of a small oral opening situated on the ventral side of the body leading into a thin walled tube, which from a lateral view resembles a stretched out S, and extends only about two thirds of the distance to the ventral sucker. The inner end is dilated to form a blind pouch. It is doubtful if the digestive system ever functions in this organism.

The excretory system consists of two pairs of flame cells for the body, and one pair for the tail. This is typical of all mammalian schistosome cercariae. Capillary canals from these flame cells join to form



CERCARIA OF S. JAPONICUM.

collecting tubules on each side which open into an excretory bladder, situated just above the junction of the body and the tail. From this excretory bladder a single tubule extends through the entire length of the tail, and bifurcates just above the point of bifurcation of the tail. One branch passing through each of the furci of the tail to open at its posterior extremity.

Recently Gordon and his coworkers in Sierra Leone have described four pairs of flame cells for the body, and one for the tail. In the cercariae of both S. haematobium, and S. mansoni. The cercariae, in this species, possess one prominent pyriform gland in the head, lying dorsal to the digestive tube, termed by Cort "the head gland", and five pairs of glands situated in the posterior half of the body. They are packed with

granular material and possess thick ducts leading to the anterior end and opening in the oral sucker. The latter are known as the cephalic glands, and form an important point of distinction between the cercariae of the three types of human schistosomiasis. The secretions from these glands are powerfully proteolytic in action, and assist the larvae in penetrating the skin of the definitive host. Takahashi (1928),⁶

is of opinion that the head gland has no secretory function, and has renamed it as the head sac. All attempts at differentiation of the sexes amongst cercariae on the basis of differences in


Recently Mohammed examined serial sections of single cercariae of S. haematobium, and S. mansoni.


size or structure have been unsuccessful. It has however, been proved that all cercariae from one snail, if allowed to infect an animal, usually develop into adult worms of only one sex, therefore the differentiation of the sexes most probably takes place in the miracidium (Cort)⁴.

The genital system in the cercariae consists of a cluster of small granular cells situated behind the ventral sucker.

Anterior to the ventral sucker, is situated a primitive nerve ganglion, which divides into two branches. According to Takahashi⁶ there are sensory organs scattered all over the body and the tail.

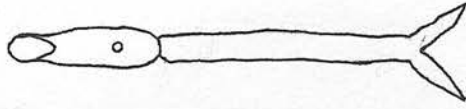
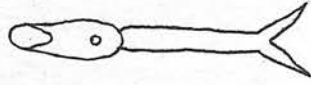
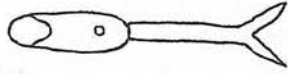
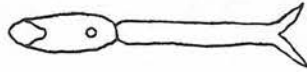
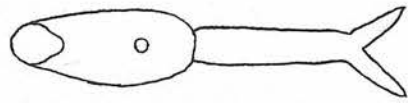
(ii) and (iii). The cercariae of S. haematobium, and S. mansoni are similar to those of S. japonicum in general structure and appearance. The main points of difference are brought out in the following table:-

	<u>S. japonicum.</u>	<u>S. haematobium.</u>	<u>S. mansoni.</u>
Total length (about)	250	390	370
Body.	120	190	160
Tail.	130	200	210
Furca.	40-50	80	60
Out-line on lateral view.	Ventral sucker slightly protuberant.	Marked protrusion of ventral sucker.	No protrusion of ventral sucker.
Cephalic glands.	Five pairs small and granular, all acid.	Three pairs, large and eosinophil 	Six pairs, two large and acid, four small and basophil.

 Recently Mohammed⁷ examined serial sections of single cercariae of S. haematobium, and S. mansoni.

S. hæmatobium. *S. mansoni.* *S. japonicum.* *Cerc. indica.* *S. spindalis.*

(Type XXX)



X 100

Comparative outline of the various schistosome cercariæ.
(After Soper)

Life history of the Schistosomes:-

He confirms the six pairs of cephalic glands in the cercariae of S. mansoni as described by Faust⁸ and others, but in the S. haematobium cercariae he has described five pairs, two large oxyphil and three small basophil.

Gordon and his coworkers⁹ found only five pairs of glands in the cercariae of both S. haematobium and S. mansoni, but Faust and Hoffman¹⁰, working in Puerto Rico with S. mansoni, have again described six pairs; two anterior large-granular and four posterior fine-granular.

Life history of S. japonicum:- Not all the eggs passed in the stools of the definitive host are fully matured. Some of the eggs may be unfertilized, and others may have been passed out before having had time to mature fully. These eggs disintegrate soon after being passed out, and play no part in the life history of the parasite.

The matured egg, as already described, is light yellowish brown in colour, and contains a readily recognizable miracidium. Between the shell and the embryo there is a space in which the egg is surrounded by a fluid medium. This fluid, as it is discharged at a later stage is of considerable importance in the control of infection. In a later stage the eggs shrink due to excretion. A provision for partial protection of the miracidium when the miracidium is made in the secretion of a shell substance around the embryo. This however

Life history of the Schistosomes:-

Introduction:- Having described the morphology of the various phases in the life of the worm, it is now proposed to give a connected account of its life history. In this section the life history of *S. japonicum* will be described in detail, and may be taken as typical of the whole genus.

It is due to the efforts of workers like Miyairi, Suzuki, Leiper, Atkinson, Faust, and Meleny that we have got a clear conception of the various points in the life history of this parasite.

Life history of *S. japonicum*:- Not all the eggs passed in the stools of the definitive host are fully matured. Some of the ova may be unfertilized, and others may have been passed out before having had time to mature fully. These ova disintegrate soon after being passed out, and play no part in the life history of the parasite.

The matured egg, as already described, is light yellowish brown in colour, and contains a readily recognizable miracidium. Hatching can only take place when the egg comes in contact with a hypotonic fluid medium. This factor, as will be discussed at a later stage is of considerable importance in the control of infection. In a hyper-tonic medium the eggs shrink due to exosmosis. A provision for partial protection of the miracidium under such circumstances is made in the secretion of a mucoid substance around the embryo. This however

gives imperfect protection and the miracidia fail to survive for more than a day or two in hypertonic media. On the other hand even immature ova will swell up and burst when immersed for some time in distilled water.

As regards the optimum temperature for hatching, Faust and Meleney² carried out carefully conducted and controlled experiments and brought out the following facts:-

1. That the optimum lay some where between 30-37° C.
2. Brief periods of exposure to extreme cold retarded hatching, but did not kill the miracidia.
3. The upper limit for the viability of the eggs was about 43° C.

In average natural conditions in an endemic area the miracidia hatch out within 3-4 days of being passed out. The egg hatches by splitting along its long axis, which is the line of least resistance. After hatching, the miracidium if viable, starts active movement, and swims about rapidly by means of its cilia.

The free miracidium, when it finds itself in clear water, ascends to an area just below the surface, and swims about in that area. Faust¹ has pointed out that this is typical of the miracidium of S. japonicum, whereas the miracidium of S. haematobium swims about freely all through the water irrespective of depth. He is of opinion that

this depends on the habits of the respective intermediate hosts.

The embryo remains infective for 60-72 hours, and if it is not able to find a suitable intermediate host in that time, it dies.

In the event of a larva coming within a few mms. of the specific snail host, it attacks the body of the animal, and bores its way into it. The snail secretes a thin mucoid substance which appears to attract the miracidia. Quite a large number of miracidia may penetrate the same snail, though a stage can be reached when the snail has been infected by a certain number, and further invasion is impossible; at least for a certain number of days. The usual sites for penetration by the miracidia are the head (especially around the tentacles), and the feet of the snail. Penetration is helped by the secretions from the cephalic glands of the miracidia, which being proteolytic can dissolve the intervening tissues.

Development within the snail:- On entering the body of the snail the miracidia shed their cilia, and find their way into the lymph spaces, movements taking place by a sort of peristalsis of the body. As already stated, the secretions from the cephalic glands are proteolytic in action, and help the organism in its movements through the tissues of the host.

Being without a properly developed alimentary

system, the miracidium is dependent on its host for its nutrition during this phase in the life history of the parasite. This is provided by the absorption of lymph (in which they are bathed all the time) through the body surface of the larvae. When a larva has established itself in a suitable lymph space, further development starts as follows:-

The cephalic as well as the lateral glands disappear, and the miracidium becomes a sac like structure in which the germ cells are undergoing active proliferation. This forms the primary sporocyst.

The germ cells inside the sporocyst divide into 2, 4, 8, and so on, till each has formed a ball of cells. These ultimately elongate and develop into sac like structures which fill up the primary sporocyst till it bursts to liberate the large number of daughter (secondary) sporocysts. The occurrence of these two generations of sporocysts was established beyond doubt by Leiper and Atkinson in 1915.

If the primary sporocyst has not already found its way to the inter-hepatic lymph spaces of the host, the daughter sporocysts show migratory activity till they finally come to lie in that part or in the region of the hermaphrodite glands.

Further proliferation of the germ cells now starts within the secondary sporocysts. These develop into cercariae, and each secondary sporocyst

becomes full of rapidly developing, and maturing bifid-tailed cercariae. Thus one single miracidium is able to give rise to innumerable cercariae.

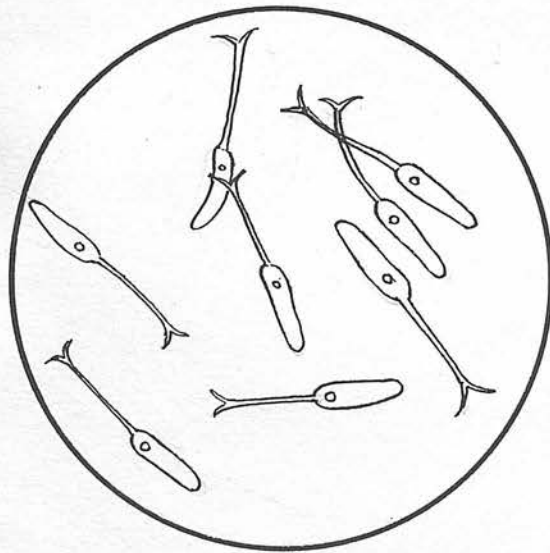
The time taken for the development of mature cercariae, averages about 8-9 weeks, from the initial penetration of the snail host by the miracidium.

As the cercariae are maturing, they burst their way through the secondary sporocyst, as well as the tissues of the snail host. Their final emergence is only seen when the snail is in contact with water. They are seen to appear singly or in groups from under the shell of the infected snail, tail first. They swim upwards, and come to rest under the surface film of the water ventral side upward.

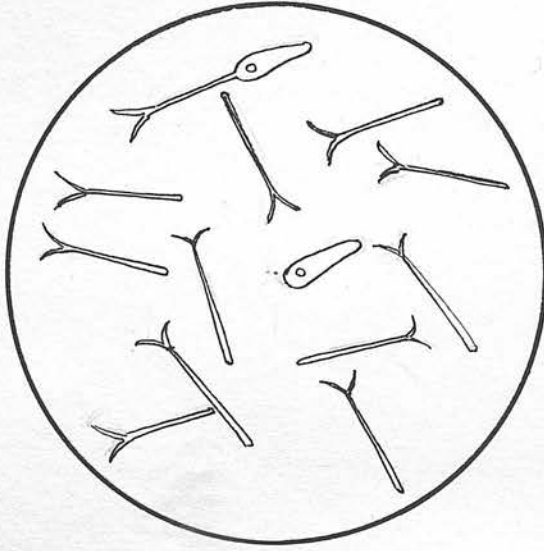
Isobe¹² found that the optimum temperature for the emergence of cercariae of S. japonicum, from the snail was 25°C; at 18-19°C they took longer to appear, and he was unable to obtain any cercariae in water below 15°C. He also found that the character of the water had no influence on their emergence, and while swimming the body always formed an angle of 30° with the horizontal.

This stage of the parasite can survive in water for a period of 24-36 hours. An abundance of oxygen appears to be essential for its survival.

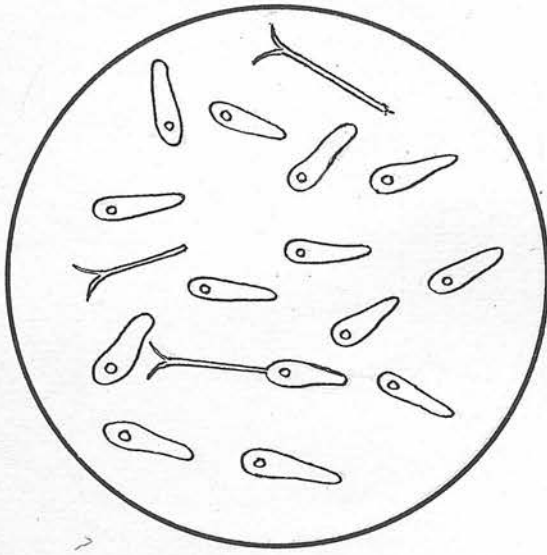
It gains access into the body of the definitive host by penetrating wet intact skin (having special preference for hair follicles), or the oral mucous



1



2



3

Skin Penetration by Schistosome cercariae.

lymph spaces, and ultimately get into the blood stream. In the blood they pass through the right heart into the lung capillaries.

As to how the worm gets from the lung capillaries to the liver, and the mesenteric veins has been greatly debated. Miyagawa and Tokimoto¹³ hold that the young worms pass on to the left side of the heart through the pulmonary veins, and are carried to the gastro-intestinal blood capillaries, from whence they find their way into the portal and the mesenteric veins. In confirmation of this view they have successfully infected three rabbits and a dog by direct inoculation of cercariae into the mesenteric artery.

On the other hand Narabayashi¹⁴ and Sueyasu,¹⁵ working independently with serial sections of infected mice have come to the conclusion that the young worms pass from the lungs to the portal veins by finding their way directly through the pleura, mediastinum, and the diaphragm.

Faust and Meleney¹⁶ employed different methods to those used by the earlier workers, and came to the conclusion that the most likely route is through the left heart and the gastro-intestinal blood capillaries. They also observed that the worms die rapidly in the gastric juice, and therefore their passage via the trachea, oesophagus, and through the stomach into the portal capillaries is impossible.

Goto (1932)¹⁷ studied this problem and concluded that both routes were possible, the results of the experimental work depending on the method employed. Faust and Meleney's method of washing the various organs of experimentally infected animals, and finding the developing worms in the washing appeared to support the theory that the worms travelled via the left heart and the arterial blood stream, whereas Narabayashi's examination of serial sections of infected mice tended to favour the view that the young worms travelled through the diaphragm.

(b) Development:- On gaining access into the body of the definitive host, the tail-less cercaria becomes a schistosomulum.

Some stages in the development of schistosomuli were described by the earlier Japanese workers but the systematic study of the subject was first taken up by Cort¹⁸ in 1921. He studied specimens obtained from experimentally infected mice, and described 18 distinct stages in the development of the schistosomulum. He was able to differentiate the sexes from the second stage onwards, so he named his stages F or M 1, and thereafter F 2-18 & M 2-18.

Faust and Meleney² repeated his experiments, using mice and rabbits, and were able to describe some stages earlier than Cort's F or M 1. They have recognized a continuous series of 24 distinct stages.

their maturity.



Growth and development of the schistosomuli starts as soon as they have found their way into the subcutaneous lymph spaces of the adult host, but the rate of growth is very slow during the period of migration to the portal blood vessels. This is easily understood because the young worm uses up most of its energy in boring its way through the tissues of the host. The rate of growth, however, becomes very brisk after the worms have arrived in the portal blood, and most of them become fully matured in about 30 days.

As the penetrating organs, namely the dorsal labia and the cephalic glands with their ducts atrophy by the fifth day, those schistosomuli which have failed to reach the portal veins by that time become tissue-locked and degenerate.

The growth and maturity rate of the worms may also be affected by:-

1. The size of the host:- It has been found that they develop much more rapidly in dogs as compared with mice; this is most probably due to the greater amount of space available in the portal system.

2. The number of worms in the portal vessels:- The growth is much quicker if an animal is infected by a small number of worms. In cases with very heavy infection, the animal may die due to the toxic effects of the worms long before their maturity.



3. Maturity stimulus of one sex on the other:-

It appears that worms belonging to both the sexes must be present in the same host before proper growth and development can take place. In cases infected with only one sex, even though all other conditions may be satisfactory the worms may live for a long time but fail to mature. Severinghaus (1928)¹⁹ found that males were normal in the absence of females, but females failed to develop in absence of males. If males arrived later, they developed and matured quite rapidly.

In suitable cases, the young worms start mating about the 15-18th. day after infection, though it takes about four weeks before they are fully matured. Fertilized eggs start appearing in the stools about the 5th week. In spite of the fact that functional maturity is reached in 4-5 weeks, the growth in size of the worms continues till about the 10th week after infection.

Before taking up the development of schistosomuli a short account may be given of the various structures in the cercaria, which have performed their function on the establishment of the larva in the adult host, and disappear during the first few days of the life of the schistosomulum:-

(i) The cuticular spines:- These were specially adopted to assist the larva in penetrating intact skin, and disappear soon after it has gained access into the body of the adult host.

from the time the worm

(ii) The tail:- This drops off a short time before or during the penetration of the skin of the host. Cort¹⁸ came across one specimen found in the blood vessels of an experimentally infected mouse three days after infection in which the tail was still attached to the body; but this is about the only instance of its kind on record, and no other observer appears to have come across a similar specimen.

(iii) The labia:- The dorsal labium becomes more prominent about the 3-4th day (this being the period of active migration in the body of the adult host), It disappears entirely by about the sixth day.

(iv) The head glands and the cephalic glands:- The head glands have been rarely seen; even in the youngest specimens of schistosomuli. The cephalic glands persist till about the sixth day. Within a short time after penetration, they become shrunken in appearance, and there is a change in their contents. Their spinous duct openings in the dorsal labium remain prominent till about the fifth day.

General growth and development:- Once the larva has found its way into the body of the definitive host it starts a very active period of growth. Within a brief period of a few weeks it grows to more than a hundred times its original size.

As already stated, the rate of growth is very slow during the first few days. The period of most active growth appears to be from the time the worm

reaches the portal blood, till about the 20th day. The rate of growth in size slows down again after the worm has attained functional maturity.

The growth of the body is restricted almost entirely to the post-acetabular region, so that the acetabulum comes to lie very near the oral sucker in the adult worm. In the male the gynaecophoric canal starts appearing about the 7th day, by growth of thin flap like structures from the post-acetabular portion of the body. By about the 17th day the flaps grow right round to overlap, and the canal is ready to receive a female. By this time the acetabulum also has grown to form the prominent, cup shaped, pedunculated structure, typical of the adult of this species.

The female grows more in length, and soon acquires the typical filiform appearance. There is a thickening of the integument over the entire length of the body, making it circular instead of oval in cross section. After the reproductive organs are developed, the post-ovarian region of the body becomes wider than the pre-ovarian. The pre-acetabular region becomes narrower as compared with the rest of the body.

Development of the alimentary system:- The inner end of the blind gut in the schistosomulum starts enlarging, and shows indication of branching into two lateral caeca, as early as the third day. At this stage some granular material may be seen inside.

The anterior end comes to lie in the centre of the oral sucker, and about the fourth day the intestinal caeca are seen to contain R.B.Cs. By the time the worms have established themselves in the portal system, the gut appears to start functioning, and is seen to contain some dark brown pigment in addition to the red blood corpuscles.

The two caeca become larger and extend posteriorly. About this time the oesophageal glands develop behind the oral sucker, and the anterior elongated part of the gut extends as far down as the acetabulum.

The caeca grow right round the acetabulum, and extend to within a short distance of the posterior end of the worm. About the 12th day the caeca reunite, and the combined gut starts growing posteriorly as the worm grows in length.

By the time the worm is fully grown the gut bifurcates at the level of the acetabulum, and reunites at the junction of the anterior $\frac{3}{4}$ with the posterior $\frac{1}{4}$ of the body of the worm. The united gut ends blindly within a short distance of the posterior end.

The excretory system:- The second flame cell of the posterior group in the cercaria drops off with the tail, so the young schistosomulum contains only three flame cells on each side of the body. As the excretory pores also are gone with the tail, the opening of the capillary tube at the posterior end

which originally led to the tail now functions as the excretory pore.

The remaining anterior flame cell of the posterior group divides into two about the third day, bringing the total to two pairs on each side as in the cercaria, with the only difference that they are all situated in the body now. About the 4th day there is a complete dichotomous division of all the flame cells and the excretory capillaries. These divisions continue as the worm develops till eventually each one of the large number of flame cells has become very small in size, and the excretory capillaries form an elaborate net work uniting into common collecting tubules.

These tubules open into a small triangular bladder, in the adult which opens on the posterolateral aspect of the worm. All the larger canals and tubules become ciliated.

The reproductive system:- This develops from the group of germ cells lying posterior to the acetabulum in the cercaria. The earliest stages in the development of this system have been described by Cort.

The nervous system:- This develops from the primitive nerve centre, which was situated anterior to the acetabulum in the cercaria. This relationship of position is maintained in the adult and the nerve ganglion comes to lie behind the oesophagus, anterior to the ventral sucker. The two lateral cords develop from the lateral branches seen in the cercaria. of the worms about 30 days after infection.

(c) Deposition of ova in the tissues of the

In the female, in the early stages there is a distinct space distinguishable in front of the point of exit of ova from the body were studied by Fairley and Manson Bahr from observations upon experimentally infected monkeys whose mesentery had been exposed day after infection. At this stage the outline of the vitelline ducts, and the uterus could also be

made out. Eggs appear in the uterus about the 30th day. According to these observers the ova are deposited in blood vessels, and a definite mechanism determines their egress to the peri-vascular tissues.

Spermatogenesis:- Linder²⁰ first described the spermatogenesis in S. haematobium. Faust and Meleney² examined sections of adult males of S. japonicum fixed in Flemming's stronger chrome-acetic-csmic fluid and stained in iron-alum-haematoxylin. They came to the conclusion that, in this species, the only difference as compared with Linder's findings in S. haematobium is that the reduced number is 8 and 7, and not 8 and 6, indicating a specific difference in the chromosome complex of these two species. They are also of opinion that the group with 8 chromosomes constitutes a female cell, and the one with 7 chromosomes a male.

The nervous system:- This develops from the primitive nerve centre, which was situated anterior to the acetabulum in the cercaria. This relationship of position is maintained in the adult and the nerve ganglion comes to lie behind the oesophagus, anterior to the ventral sucker. The two lateral cords develop from the lateral branches seen in the cercaria. till about ten or more ova have been laid in the same

(c) Deposition of ova in the tissues of the host:- The nature of this process, and also the method of exit of ova from the body were studied by Fairley and Manson Bahr²¹ from observations upon experimentally infected monkeys whose mesentery had been exposed under anaesthesia.

According to these observers the ova are deposited in blood vessels, and a definite mechanism determines their egress to the peri-vascular tissues. When the time for oviposition arrives the paired worms travel towards the intestine, against the venous blood stream to the farthest possible point in the sub-mucosa. Here the female leaves the male, and being more slender it can pass on into much smaller venules. Its progress at this stage is aided by its great power of elongation, and the muscularity of the body; the suckers prevent it from being washed back by the blood stream. This progress is continued till it has completely plugged a small venule with its body, and is not able to move on any further. This produces stasis and oviposition is soon commenced.

The ova are ejected through the vaginal opening, situated behind the ventral sucker. The female then withdraws a little and the blood vessel contracts on the ova, preventing their flowing back with the blood. After receding a little the female ejects some more ova, and withdraws a little further back again, the process being repeated several times till about ten or more ova have been laid in the same

venule.

Another point of differences between the three Faust and Meleney made some observations on types of human schistosomiasis is, that in case of experimentally infected dogs and brought out the S. haematobium twenty or more ova may be deposited in following differences from Fairley's findings:- the same venule, but the maximum number recorded in

1. In case of S. japonicum the female never leaves the male, right up till the time of oviposition, and they can migrate right down to the submucosa may appear in the stools as early as a fortnight before their appearance in the urine; this is most probably

2. They found some large groups of ova due to the worms taking longer to reach the vesicular (100-200) of S. japonicum in the intestinal mucosa venous plexus, and submucosa in these dogs, and came to the conclusion that in the case of this species a female may excites an inflammatory response resulting in an deposit all most all the ova in its uterus, including the immature ones.

The ova appear to elaborate a toxin which infiltrates the surrounding tissues with leucocytes, mainly eosinophils and polymorphonuclears. Brumpt (1931)²² is also of opinion that the female does not leave the male at the time of oviposition. According to him the male plugs the blood vessel, and there is no grasping of the ova by the found chiefly in the walls of the large intestine, walls of the blood capillaries.

In cases infected with S. japonicum the ova are but inspite of the elaborate mechanism some of them are washed back into the blood stream and may find the passage of the ova through the walls of the their way into the mesenteric glands, the liver, the blood vessels is probably aided by their spines; spleen, or the pancreas. In rare cases they find though their final passage through the walls of their way into the systemic blood stream, and get the bladder or the intestine as the case may be arrested in any other organ or tissue. In some cases appears to be by ulceration through the tissues. the ova have been found to form emboli in the spinal According to Brumpt the spine plays no part in the cord or the brain, producing symptoms of nervous passage of the ova through the walls of the blood disease.

vessels. In S. japonicum the entire passage from All ova which fail to find their way into the the venule in which the ova are laid to the lumen of the intestine have reached a cul-de-sac, and of the intestine is by an ulcerative process. are unable to play any further part in the life history

Another point of differences between the three types of human schistosomiasis is, that in case of S. haematobium twenty or more ova may be deposited in the same venule, but the maximum number recorded in the case of S. mansoni is six.

In cases with S. haematobium infection some ova may appear in the stools as early as a fortnight before their appearance in the urine; this is most probably due to the worms taking longer to reach the vesicular venous plexus.

The ova appear to elaborate a toxin which excites an inflammatory response resulting in an infiltration of the surrounding tissues with leucocytes, mainly eosinophils and polymorphonuclears. This is followed by ulceration resulting in the passage of the ova towards the lumen of the gut.

In cases infected with S. japonicum the ova are found chiefly in the walls of the large intestine, but inspite of the elaborate mechanism some of them are washed back into the blood stream and may find their way into the mesenteric glands, the liver, the spleen, or the pancreas. In rare cases they find their way into the systemic blood stream, and get arrested in any other organ or tissue. In some cases the ova have been found to form emboli in the spinal cord or the brain, producing symptoms of nervous disease.

All ova which fail to find their way into the lumen of the intestine have reached a cul-de-sac, and are unable to play any further part in the life history

of the parasite.

Perry²³ is of opinion that in the case of S. haematobium, the passage of the ova, even through the mucosa is dependent on the use of the spine, and he has produced some microphotographs in support of this view.

and later on... the Katayama... established that the... all the five... of the genus Katayama.

Annandale²⁴ suggests that the generic name for these snails is Blanfordia (Gredler), and Katayama, and Hamada give the sections, depending on whether the body is smooth or with vertical ribs. He classifies them as follows:-

Shell smooth:- (Katayamae).

(1) Complete shell less than three times as high as it is broad:- B. formosana.

(2) Complete shell more than three times as high as it is broad:- B. nasophora.

Shell with vertical ribs:- (Hemibae).

(A) Ribs not prominent:- B. sublaevis.

(B) Ribs prominent:-

(1) Shell more than nine inches high:- B. longicosta.

(2) Shell less than eight inches

high:- B. hypensis.

²⁴Esquart considers Oncamelania, Hypocbia, Hemibae, and Katayamae as synonyms of Blanfordia.

The intermediate hosts:-

1. The parasites and their incriminated carriers:-

(a) S. japonicum:- The intermediate host of S. japonicum was first discovered by Miyairi and Suzuki in 1913, on the island of Kyushu in Japan, and later on confirmed by Leiper and Atkinson in the Katayama endemic area. It has been definitely established that the snail hosts of S. japonicum in all the five endemic areas in Japan are members of the genus Katayama.

Annandale²⁴ suggests that the correct generic name for these snails is Oncomelania (Gredler), and Katayama, and Hemibia are its sections, depending on whether the body is smooth or with vertical ribs. He classifies them as follows:-

Shell smooth:- (Katayamae).

(A) Complete shell less than three times as high as it is broad:- O. formosana.

(B) Complete shell more than three times as high as it is broad:- O. nosophora.

Shell with vertical ribs:- (Hemibae).

(A) Ribs not prominent:- O. sublaevis.

(B) Ribs prominent:-

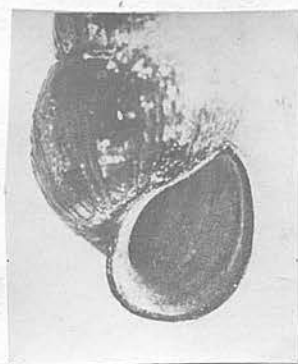
(i) Shell more than nine inches

high:- O. longiscata.

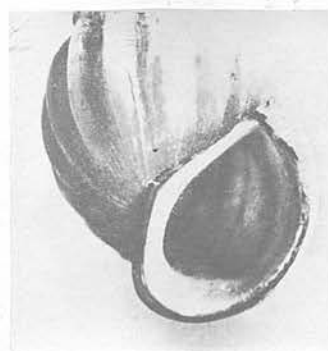
(ii) Shell less than eight inches

high:- O. hupensis.

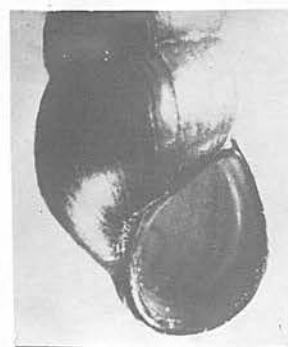
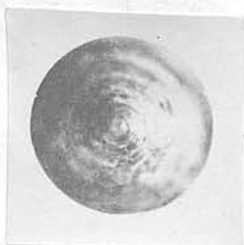
Bequaert⁴⁴ considers Oncomelania, Hypsobia, Hemibiae, and Katayamae as synonyms of Blanfordia



ONCOMELANIA NOSOPHORA.



ONCOMELANIA HUPENSIS.



ONCOMELANIA FORMOSANA.

SNAIL HOSTS OF SCHISTOSOMIASIS JAPONICA.

(Adams) 1863. Pilsbry⁴⁵ adds that as *Blanfordia* is found as far North as Yesso, possible hosts of *S. japonicum* exist all over Japan.

According to Annandale, probably all the known and unknown species of *Oncomelania* are potential carriers of *S. japonicum*. The shell in all these snails is long and narrow with many whorls and the breadth increases gradually from the pointed apex downwards. The two basal whorls are about the same size. The sculpture on the surface is arranged in vertical lines. The mouth of the shell is ovate, pointed above, and broadly rounded below. The operculum which closes the shell is very thin and transparent, of ovate outline, and with a small spiral figure on the inner side towards the base.

The snail itself has a short snout, bilobed in front which does not assist in locomotion. It has two fine tentacles, one on either side of the head, with an eye situated near the base of each. The foot on which the animal crawls is broad and short, rounded behind and truncated in front. In Japan, the snails belonging to the genus *Blanfordia* closely resemble the *Oncomelania* snails, so far as the shell and the operculum are concerned. The apex of the shell of *Blanfordia* is comparatively blunt and flat, there is no thickening on the inner surface of the lip as in *Oncomelania*, and the number of whorls is smaller. The main difference in the

snail itself is that the *Blanfordia* snails have a long narrow, highly extensile snout which helps in locomotion. Langeron found that the intermediate host of

In China, the *Oncomelania* snails can be easily distinguished from some of the local species in the various areas. *Opeas gracile* (Hutton), and the allied species that occur in China are non-operculate and their eyes are borne at the ends of slender tentacle like stalks, arising from the side of the short, tubercle like true tentacles.

Some of the smaller members of the genus *Melania* may some times be difficult to differentiate from *Oncomelania*. They are usually much bigger in size, and the vertical ribs in the shell (which make them resemble the *Oncomelania* snails) are traversed by horizontal grooves..

Amongst other snails which may possibly cause confusion, with *Oncomelania* are those belonging to the genera *Tricula*, *Delavaya*, *Paraprososthenia*, and *Parapyrgula* in Yunnan and Szechuan, and the genus *Pachydrobia* in French Indo-China. The former group have no varix on the lip, and the latter have a thick calcareous operculum, marked externally with concentric lines.

(b) *S. haematobium*: - Leiper, in 1915, traced the infection to the snails belonging to the genus *Bullinus* implicating *B. contortus*, *B. dybowskii*, and *B. innesi*. These are sinistral and spiral snails. In 1916, Becker added *Physopsis africana* to the list,

and in 1920, Anne Porter²⁶ found the typical cercariae in Limnea natalensis in South Africa.

Langeron²⁷ found that the intermediate host of S. haematobium in Tunis was Bullinus brochii, and Dye²⁸ incriminated a snail called Melania nodocincta Dohrn in Central Africa. In Portugal, Bettencourt and Da Silva²⁹ have reported infection in Planorbis dufourii.

(c) S. mansoni:- The intermediary hosts for this species are flat fresh water snails belonging to the genus Planorbis. Leiper incriminated P. boissyi in Egypt in 1915. Lutz³⁰ (1917) showed that in Brazil P. oliveaceus was the carrier, and the same species was also found to be the intermediate host in Dutch Guinea by Lee and Khalil³¹ in 1921.

Iturbe and Gonsales (1917)³² described P. guadilupenses as the intermediary host in the West Indies and Venezuela. Christopherson³³ incriminated P. centrimentalis in Brazil.

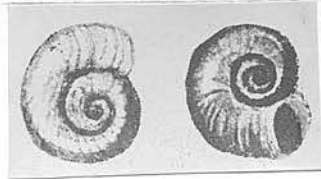
Bayliss³⁴ summarised the intermediary hosts of S. haematobium and S. mansoni in 1931 as follows:-

(1) S. haematobium:-

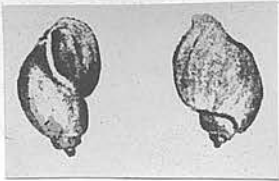
- (1) Bulinus truncatus (Audouin, 1826).
(Synonyms contortus, dybowskii etc.)
- (2) Physopsis africana (Krauss 1848).
- (3) Physopsis globosa (Morelet, 1866).
- (4) Planorbis dufourii (Graells, 1846).

(2) S. mansoni:-

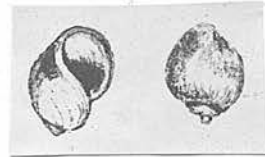
- (1) Planorbis boissyi (Potiez, 1838).
- (2) Planorbis pfeifferi (Krauss, 1848).



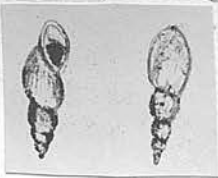
PLANORBIS BOISSYI



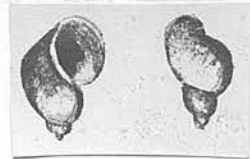
BULLINUS DYBOWSKI.



BULLINUS CONTORTUS.



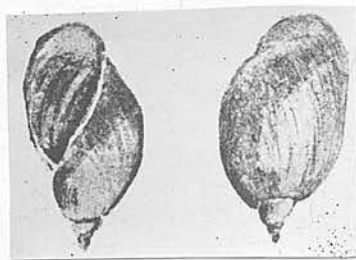
BULLINUS FORSKALI.



BULLINUS INNESI.



LIMNEA TRUNCATULA.



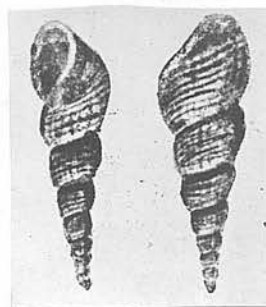
LIMNEA CAILLAUDI.



BYTHINIA SENAARICA.



PHYSA SUBOPACA.



MELANIA TUBERCULATA.

found in the (3) Planorbis olivaceus (Spix, 1827).

Planorbis, (4) Planorbis guadeloupensis (Sowerby, 1821).

they contained other cercariae could not be infected experimentally with the miracidia of S. japonicum.

(5) Planorbis centimetralis (Lutz, 1918).

(6) Planorbis antiguensis (Sowerby, 1877).

(7) Physopsis africana (Krauss, 1848).

(8) Bulinus tropicus (Krauss, 1848).

2. Distribution of intermediate hosts:- In Japan according to Annandale²⁴ Oncomelania snails occur in the Southern half of the archipelago, where their distribution appears to be some what sporadic.

Oncomelania formosana is found in Formosa.

The genus Oncomelania is widely distributed in China, except in the extreme Northern and Western provinces.

Faust and Meleney³⁵ made an attempt to find the intermediate hosts of S. japonicum in the various parts of China. As Faust had already found that the miracidia of S. japonicum, on emerging from the ova, were restricted to an area just below the surface film of water, they searched for snails with similar habits. Their search was conducted in three areas in central Eastern China, and one in Southern China. They found that:-

1. In the Souchow area (Kiangsu province), a small operculate snail 4.2-9 mm. in length and 2.1-3.8 mm. in breadth, identified as Oncomelania hupensis acted as the intermediate host. They were successful in experimentally infecting these snails with miracidia obtained from a dog infected with Schistosoma japonicum in Japan. The other snails leading from Hsienxing to the Yangtze at Kinkow.

found in the same area, belonging to the genera *Cerastium*, *Planorbis*, *Limnea*, *Bythinia*, and *Vivipara*, though they contained other cercariae could not be infected experimentally with the miracidia of *S. japonicum*.

2. In the Kashing area, (Chikiang province), also *O. hupensis* was acting as the intermediate host. No snails belonging to the section *Katayama* were found in either of these areas.

3. In the Shahohsing area (Chikiang province) *Katayama nosophora*, harboured the parasites.

4. The Pearl River delta and the West River valley above Fatshan contained large numbers of *Katayama nosophora* snails; but these were not infected.

From the above, these observers conclude that the principal intermediate host in China is *O. hupensis*, and *K. nosophora* holds a secondary position, the exact distribution of each depending on the water supply. *O. hupensis* is found in very slow moving water whereas *Katayama* prefers the vicinity of clear flowing mountain water.

Meleney³⁶ published a further report of his findings in connection with the continued search for *O. hupensis* in China as follows:-

1. At Yochow on the shore of the Tung Ling lake, he found these snails mainly in long grass along the coves of the summer water level of the lake.
2. Near Kinkow in tall grass along a stream leading from Hsienning to the Yangtze at Kinkow.

3. In a pond and a ditch near the 7 mile Creek which encircles Hankow.

4. Near Yanglow, 20 miles below Hankow at the village of Wang Chia Tien, on the shore of a clear water lake, in moist grass.

5. Near Anking, Anhwei, in moist grass along a small stream, and along the shore of the Canal - River Nei Ho, which runs just North of and parallel to the Yangtze.

6. At Puko, Kiangsu, in the grass along the shore of a canal.

He comments on the gradual variation in the size and density of the shells of the snails; those from upper Yangtze area being big and hard, and those in Japan being small and soft.

Tubangui³⁷ has recently proved that Blanfordia quadrasi acts as the intermediate host of S.japonicum in the Phillipine islands. He found cercariae, morphologically indistinguishable from those of S.japonicum in these snails, and was able to obtain the typical adult worms by infecting rabbits and monkeys with these cercariae.

The genus Bullinus and its allied species have a fairly wide range in Africa, and have been reported from North, West, and South Africa, Abyssinia and South Europe.

The range of the genus Planorbis is wider still, being widely distributed in the tropics and the sub-tropics.

3. The habitat of the intermediate hosts:-

Usually these snails are found in stagnant or slow moving water, or else in its neighbourhood. There are certain variations depending on the species and the local conditions in the particular area.

The *Oncomelania* snails are usually found close to the edge of clear, relatively still, fresh water. They are most abundant on the banks, within about two feet of the water edge. They may also be found on the stalks of water grass, a few inches above or below the surface.

According to Kan and Yao³⁸ the *Oncomelania* snails are amphibian. In the wet season they live in water but in the dry season they are found under grass and stone pieces in moist soil. They are not buried in the mud.

In China they are found to be most abundant in the small terminal canals, and the nursery rice beds; the rice fields being comparatively free.

Out of the two African genera of snails *Bullinus* and *Physopsis*, the former is usually found in the irrigation canals, and the village ponds and 'Birkets', whereas the latter is more often found in mud and sewage. Occasionally *Physopsis* snails may be found in bathing pools.

The *Planorbis* snails vary according to the species. Some species e.g., *P. guadeloupensis* thrive best in the beds of rivers, and in the irrigation canals. *P. oleveacicus* prefers stagnant pools and

mud where there is plenty of vegetation. P. exustus is usually found in stagnant ponds and tanks.

P. boissyii is found in the smaller irrigation channels in Egypt.

4. The infected snail:- Leiper first remarked that an infected Planorbis snail could be easily recognised at a glance on account of its increased bulk, and the change of the colour of the digestive glands from dark brown to ochre.

According to Fairley an infected snail may be distinguished macroscopically by the greater friability of its shell, and the change in colour.

Lutz observed a considerable state of marasmus in infected snails which according to him limits their life to about three months. Soparker³⁹ found that it was difficult to keep the infected snails alive for more than a few days.

5. Breeding season:- According to Kan and Yao the Oncomelania snails conjugate in March and April, and oviposit in May. Bullinus snails breed during July and August, and Planorbis during April and May (Manson Bahr and Fairley).

6. Study of the snails and the cercariae harboured by them in Bombay:- Several ponds, swamps, tanks, and drains in, and around Bombay were searched for snails. The sites included some of those mentioned by some of the previous workers viz. Sewell (1922)⁴⁰, Soparker and Liston (1917)⁴¹, and Fairley and his coworkers (1930)⁴². Some new places as shown in the following table were also visited:-

Sewell (1922) :-

1. Swamps at
 - (a) Mahim and
 - (b) Bandra.

Liston and Soparker (1917) :-

1. Swamps at Bandra.
2. Ponds at
 - (a) Santacruz,
 - (b) Andheri, and
 - (c) Khar.

Fairley and Jesudasan (1930) :-

1. Shemuru.
2. Santacruz.
3. Andheri.

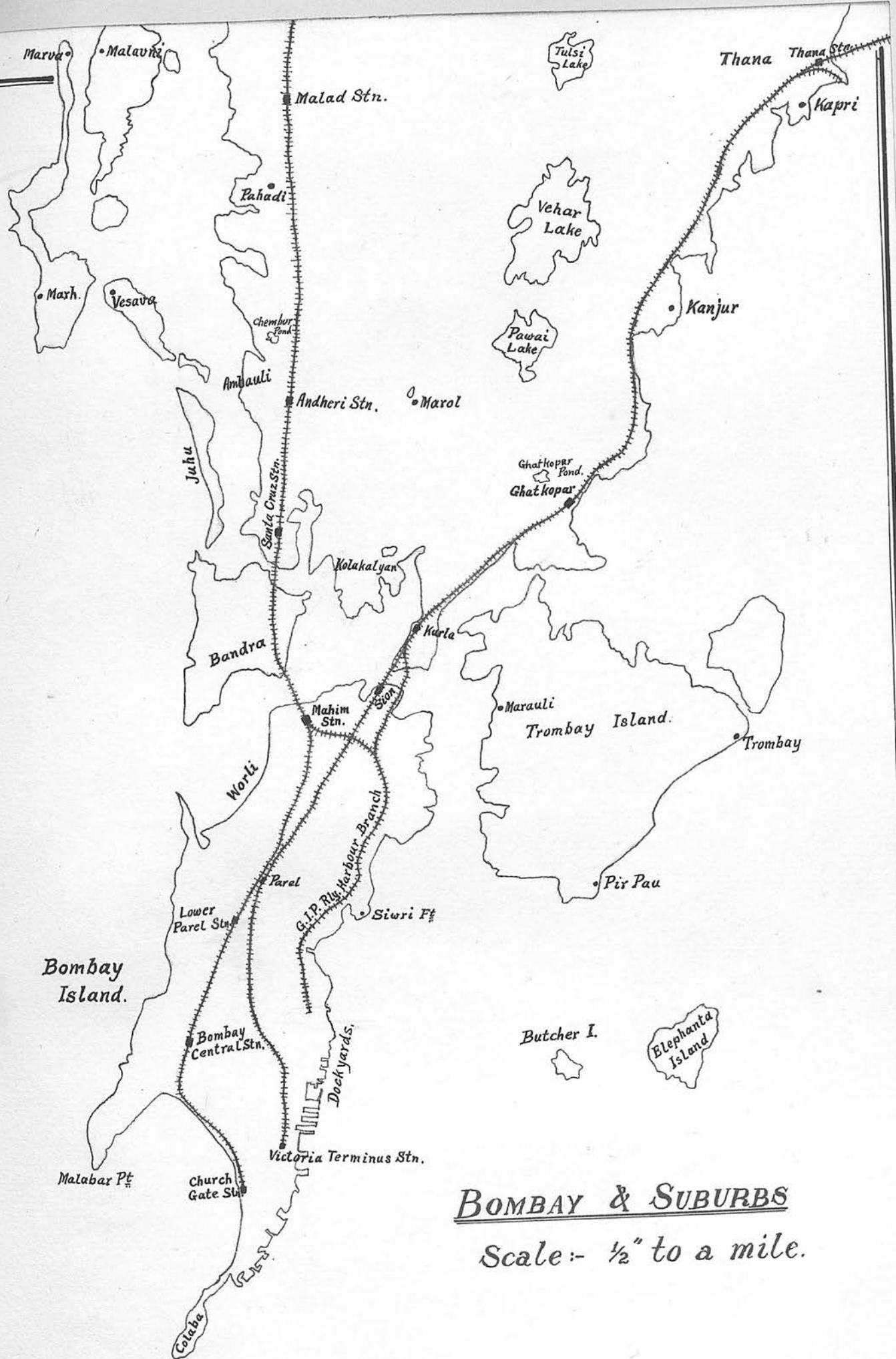
Writer (1933-35) :-

1. Swamps along Sewri, Wadala, and Kurla.
2. Ponds at
 - (a) Wadala.
 - (b) Chembur.
 - (c) Khar.
 - (d) Jogeshawari, and
 - (e) Ghat kopar.
3. Open drains along
 - (a) Harbour line (G.I.P. Railway),
 - (b) Dadar, and
 - (c) Dharavi.
4. Lakes
 - (a) Powai, and
 - (b) Vihar.

Inspite of quite an extensive and thorough search being made in the above mentioned localities only the following five species of fresh water snails were encountered.

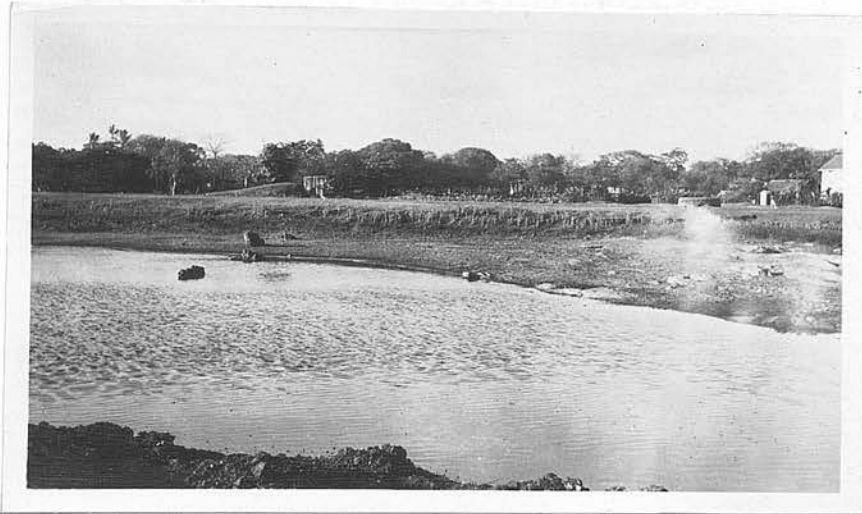
1. Vivipara bengalensis:- Powai and Vihar lakes and Swamps at Bandra, Chembur and Ghat kopar.
2. Indoplanorbis exustus:- Open drains and ponds at Wadala, ponds at Khar, and Jogeshawari, and Swamps at Dharavi.

3. Limnea acuminata:- These were found mostly along the Harbour branch line (G.I.P. Railway), but were in much smaller numbers as compared with 1 and



BOMBAY & SUBURBS

Scale:- $\frac{1}{2}$ " to a mile.



Fresh-water Pond at Chembur.



Fresh-water Pond at Chembur



Fresh-water Pond near Ghat-Kopar.



Fresh-water Pond near Ghat-Kopar.

- careful 4. Melanoides tuberculatus:- Mahim and Bandra swamps. snails which had not passed out any cercariae by the 5. Pachylabra globosa:- Wadala and Mahim swamps.

According to Preston (1915)⁴³, no less than 21 different species of fresh water snails should be found in the Bombay presidency but his list includes several snails which are known to have a world wide distribution, though they have not yet been found in the locality under investigation.

It was found that the best time for collecting the snails was in the early morning, just before sunrise, when most of the snails were found floating in the water or attached to stones or weeds just below the surface. After sun-rise most of them buried themselves in the mud at the bottom of the ponds and were hard to find. The infested ponds and swamps were usually easy to spot because of the large number of empty shells of the snails that were strewn along their banks.

A large number of specimens of each species were first examined for infection with any furcocercous cercariae similar to those belonging to the three types of human schistosomiasis. The snails were collected in a wide mouthed jar filled with water from the same pond, and later on washed in tap water to free them from mud. They were then put into test tubes (one in each) containing a few c.c. of clear tap water at ordinary room temperature.

Though most of the snails started passing out cercariae within a few minutes, all the tubes were

III. L. acuminata.

IV. M. tuberculatus.

V. P. Globosa.

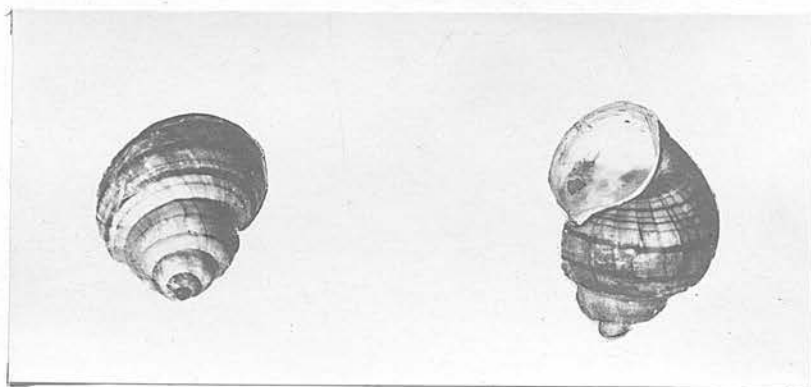
carefully examined with a hand lens after 24 hours. Those snails which had not passed out any cercariae by that time were considered to be uninfected.

The following table gives a summary of the infected ratio of the various species of snails over a period of six months with all types of cercariae:-

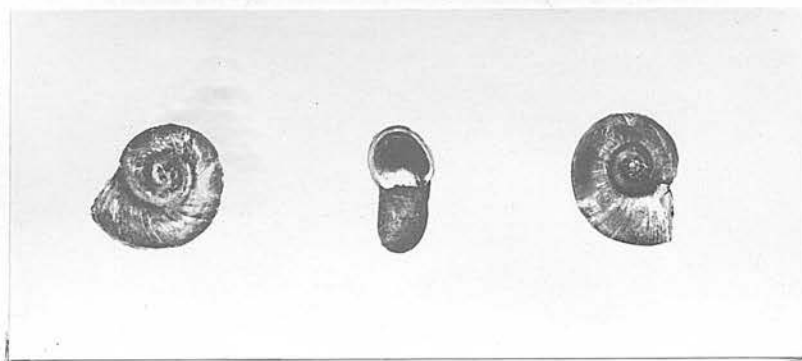
Snail.	Year 1933-34.							Per cent
	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Total	
I	Exam-ined.	35	43	32	38	42	40	230
I	Infec-ted.	Nil	Nil	Nil	Nil	Nil	Nil	Nil
II	Exam-ined.	41	38	55	32	42	47	255
II	Infec-ted.	34	30	42	21	29	42	198
III	Exam-ined.	25	18	22	27	19	23	134
III	Infec-ted.	9	11	8	12	7	10	57
IV	Exam-ined.	17	15	12	14	15	12	85
IV	Infec-ted.	3	4	1	2	7	3	20
V	Exam-ined.	10	11	9	11	12	7	60
V	Infec-ted.	4	3	2	0	1	0	10

I. V.bengalensis
 III. L.acuminata.
 V. P.Globosa.

II. I.exustus.
 IV. M.tuberculatus.



VIVIPARA BENGALENSIS.



PLANORBIS EXUSTUS.

PLANORBIS EXUSTUS.



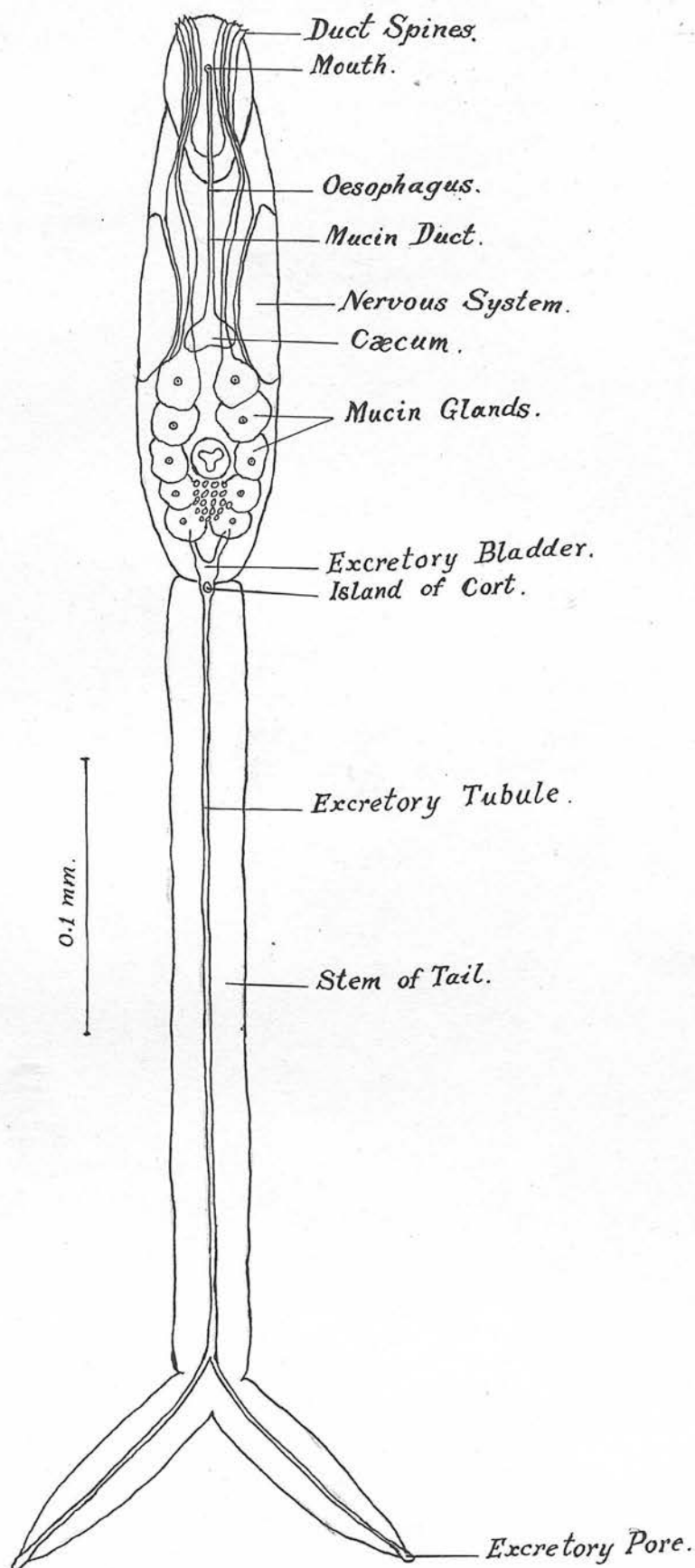
ACTUAL SIZE.

A few of the cercariae were furcocercous, and these were set aside for more careful examination. A large proportion of these were again found to possess prominent dark pigmented eye spots leaving a very small group which could possibly belong to the human or animal types. Most of the remaining cercariae measured about .5 mm. in length and on careful examination were found to resemble the cercaria of S. spindalis as described by Soparker. This cercaria was obtained from Indoplanorbis exustus, or rarely Limnea acuminata snails.

As most of the snails were infected with more than one species of parasite it was not possible to try transmission experiments.

An attempt was also made to find the seasonal infective index of the I. exustus snails collected from a pond at Chembur, and an other one at Dharavi with this cercaria. Unlike the other observers an equal number of snails from each pond was obtained each month for a period of fifteen months, and examined for infection. By this means it was possible to obtain a proportional idea of infection from a random sample of fixed strength from a population of a few thousand snails from month to month. The results are shown in the following tables and curves.

CERCARIA OF S. SPINDALIS.



CERCARIA OF *S. SPINDALIS*.

Seasonal infective index of Indo-planorbisexustus snails collected from ponds at:-

Charts showing the seasonal infective index of

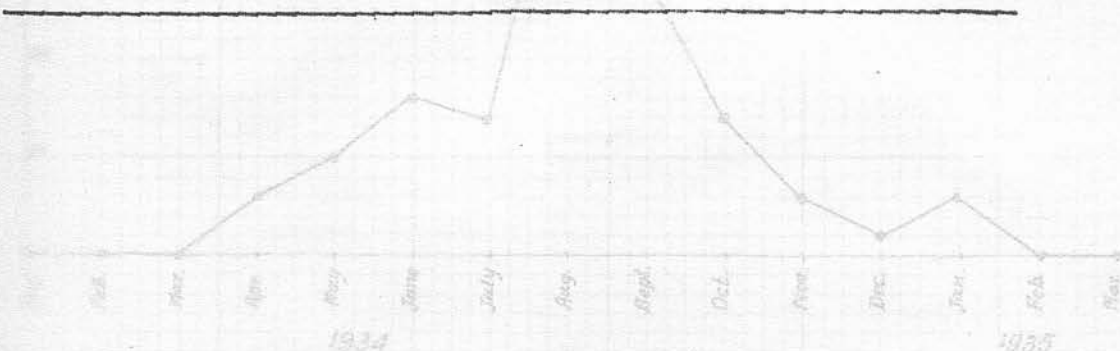
Month	(a) Chembur.			(b) Dharavi.		
	Exam- ined.	Infec- ted.	Percentage Infected.	Exam- ined.	Infec- ted.	Percentage Infected.

1934.

Jan.	50	1	2 %	50	-	-
Feb.	"	-	-	"	-	-
Mar.	"	-	-	"	-	-
Apr.	"	1	2 %	"	3	6 %
May.	"	2	4 %	"	5	10 %
June.	"	9	18 %	"	8	16 %
July.	"	20	40 %	"	7	14 %
Aug.	"	18	36 %	"	23	46 %
Sept.	"	27	54 %	"	14	28 %
Oct.	"	23	46 %	"	7	14 %
Nov.	"	11	22 %	"	3	6 %
Dec.	"	2	4 %	"	1	2 %

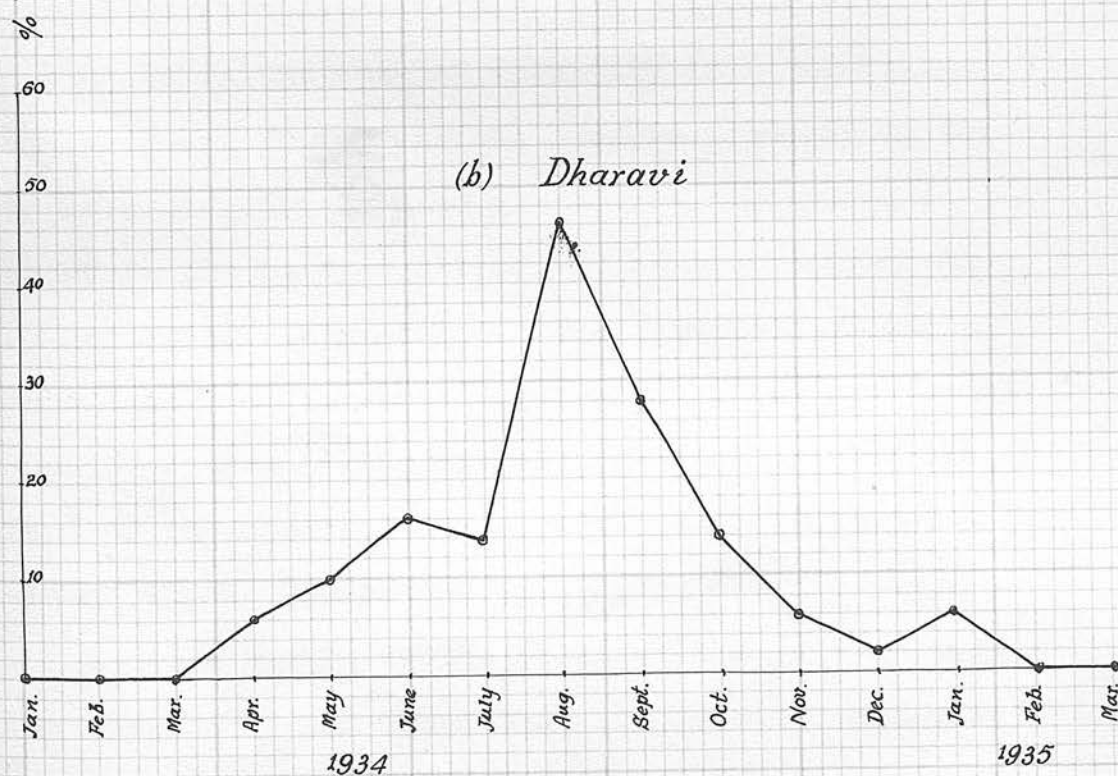
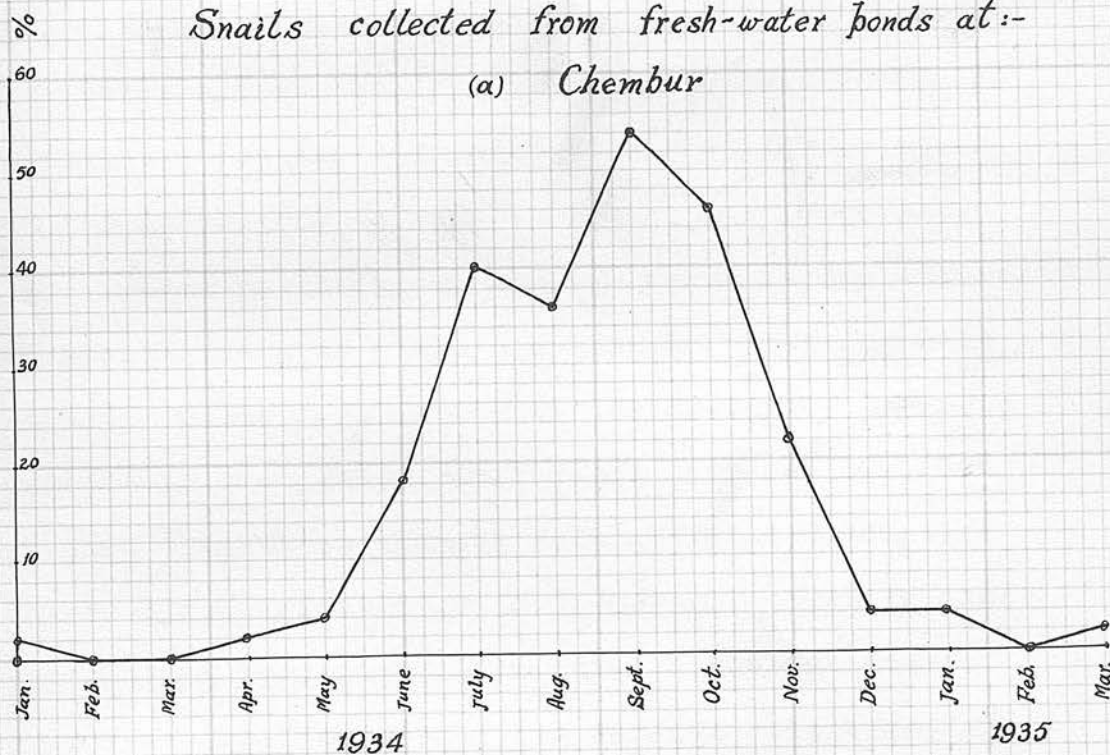
1935.

Jan.	"	2	4 %	"	3	6 %
Feb.	"	-	-	"	-	-
Mar.	"	1	2 %	"	-	-



Charts showing the seasonal infective index of
I. exustus snails with *S. spindalis*.

Snails collected from fresh-water ponds at:-



Pathology of schistosomiasis:-

Introduction:- In this section it is proposed to discuss the various changes produced in the organs and tissues of the adult host due to infection with these worms. These changes vary greatly in their character and degree depending on the species of the parasite infecting the individual, and the duration of the infection.

Some pathological changes found in the tissues of people dying of 'Katayama disease' (the Japanese name for schistosomiasis) were described by Japanese workers in the latter part of the 19th century, but at that time these changes were attributed to other causes e.g., infection with Clonorchis sinensis, and Paragonimus westermani. In 1904, Katsurada⁴⁶ made a survey of the findings of the various observers up-to-date and recognised the relationship of these pathological changes with S. japonicum.

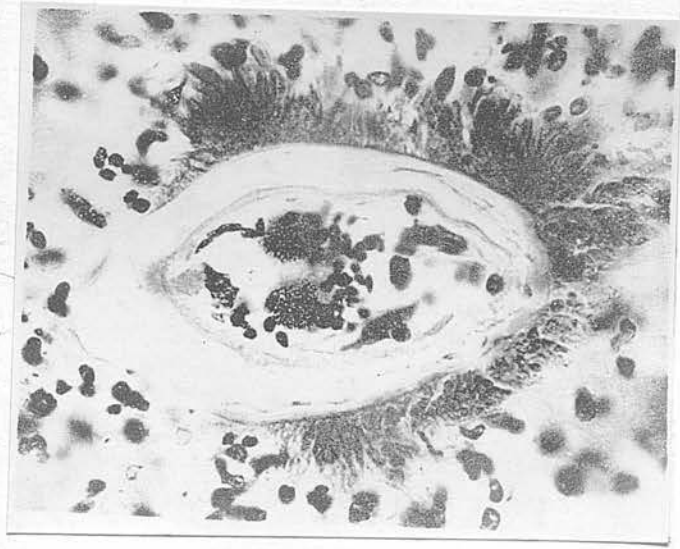
As in the case of infection in human beings observations of the various lesions produced by the worms could only be made on autopsy, the changes found in the late stages of the disease only could be described. Therefore further progress of our knowledge of this subject, especially as regards the earlier stages of the disease was held up till the days of the study of the experimentally infected animal in the laboratory.

As a result of the observations made by the various workers on experimentally infected monkeys, dogs, rabbits, mice etc., we have now got a complete

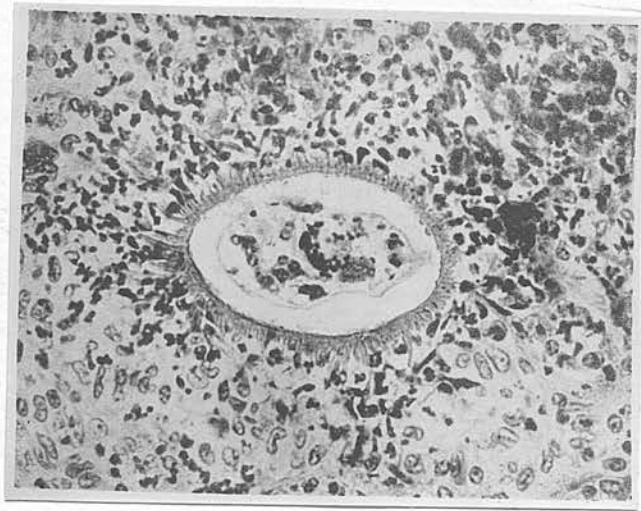
picture of the effects produced by these worms on the organism of the adult host. Small differences of opinion that exist between different observers will be brought out when the particular problems are under discussion.

Though there has been considerable dubiety on the subject, there appears to be no doubt that in addition to the changes produced by the worms and their ova by acting as foreign bodies in the system, there are other changes which must be due to the action of some toxic materials elaborated by the parasites. Kiyono and Murakami⁴⁷ injected various foreign substances e.g., oil drops, starch granules, and lycopodium spores in the livers of animals and compared the tissue reaction set up by these substances with that produced by the ova of S. japonicum. They came to the conclusion that the reaction around the ova was much more intense. They also found that as the eggs die the reaction around them becomes less marked and slowly disappears. In their opinion the ova secrete some poisonous material which sets up an intense tissue reaction around them and ultimately helps in their extrusion through the walls of the intestines by dissolving the intervening tissues.

The above view has been further supported by the comparatively recent work of Hoeppli⁴⁸ in which he has brought out the fact that there is an eosinophilic staining secretion found around the ova which appears



*Rabbit's Lung S. japonicum ,
Schistosoma Egg Showing Secretion
Through the Egg~Shell.*



*Rabbit's Lung S. japonicum,
Schistosoma Egg Showing Secretion
Through the Egg~Shell Surrounded
by Polymorphonuclear Leucocytes.*

to excite a marked reaction in the surrounding skin disease known as 'Kabure' which is prevalent in tissues in rabbits, which tends to disappear if the some parts of Japan is due to invasion of the skin by eggs are destroyed by treating the infected animal the cercariae of *S. japonicum*. This disease is with injections of Fouadin. He also noticed that characterised by a flea-bite like papular eruption the fibrosis around the living eggs was much more accompanied by itching which disappears in 4-5 days, marked as compared with that around the dead ones. In view of the following facts it appears unlikely

Hutchison⁴⁹ is of opinion that these worms that this has any connection with schistosomiasis:- and their ova can induce a primary inflammatory

(i) Cases of this disease have been seen in reaction but they have no inherent capacity to certain areas in Japan where schistosomiasis is produce suppuration; the latter depending solely on unknown.

secondary bacterial invasion. Abscess formation has

(ii) There is no mention of this eruption by not been seen in the deeper tissues or the abdominal any of the observers in the various parts of China, organs. The reaction around the ova, where not where schistosomiasis is endemic.

modified by secondary bacterial invasion, is similar

(iii) Miyagawa examined a large number of sections to that excited by a foreign body, though it is much from the papules and the surrounding skin in

more intense. The surrounding tissues are first cases of 'Kabure' but failed to find any schistosome infiltrated by inflammatory leucocytes, and later on cercariae. He also immersed his arm in rice-field fibroblasts and giant cells appear. The appearance water, and developed the typical eruption without now becomes that of a granuloma, not unlike a tuber- becoming infected with *S. japonicum*.

culous nodule. The characteristic feature, however,

There is no doubt however, that invasion of consists in a preponderance of eosinophil leucocytes the skin by the cercariae of *S. japonicum* is often in these nodes (Fairley)⁵⁰. These granulomatous pseudo- followed by an eruption. Faust and Meloney noticed tubercles in the deeper tissues are ultimately a distinct papular eruption in an experimentally replaced by fibrous tissue.

infected dog, which appeared 15 hours after infection.

The pathological effects of *S. japonicum*:-

Lee has reported a case where there was a marked

(a) During invasion:- The penetration of the papular eruption in a man after bathing in infected skin by the cercariae is accompanied by intense water, which was followed by infection with *S. japonicum*. itching of the part invaded, and in most cases this The passage of cercariae through the skin is is followed by a papular eruption which disappears accompanied by congestion of blood vessels, oedema, in 3-4 days. For some time it was believed that the

and infiltration of the surrounding skin area with skin disease known as 'Kabure' which is prevalent in some parts of Japan is due to invasion of the skin by the cercariae of S. japonicum. This disease is

(b) During migration of the parasites:- No characterised by a flea-bite like papular eruption visible pathology is produced by the young schistosomes while they are in the blood vessels. In view of the following facts it appears unlikely that this has any connection with schistosomiasis:-

(i) Cases of this disease have been seen in certain areas in Japan where schistosomiasis is unknown.

(ii) There is no mention of this eruption by any of the observers in the various parts of China, where schistosomiasis is endemic.

(iii) Miyagawa⁵¹ examined a large number of sections from the papules and the surrounding skin in cases of 'Kabure' but failed to find any schistosome. He also immersed his arm in rice-field water, and developed the typical eruption without becoming infected with S. japonicum.

There is no doubt however, that invasion of the skin by the cercariae of S. japonicum is often followed by an eruption. Faust and Meleney⁵² noticed a distinct papular eruption in an experimentally infected dog, which appeared 15 hours after infection. Lee⁵³ has reported a case where there was a marked papular eruption in a man after bathing in infected water, which was followed by infection with S. japonicum.

The passage of cercariae through the skin is accompanied by congestion of blood vessels, oedema, The latter is shared by the renal cortex, and is a

and infiltration of the surrounding skin area with most probably due to general toxæmia. A congestive polymorphonuclear, mononuclear, and eosinophil leucocytes (Faust and Meleney).

(b) During migration of the parasites:- No visible pathology is produced by the young schistosomuli while they are in the blood vessels. When they are arrested in any organ or tissue, they give rise to certain changes. The most characteristic of these as noticed in the lymph glands and the lungs, in the early stages, consist of small haemorrhages, and oedema with leucocytic infiltration of the surrounding tissues. The changes in the lungs are most marked under the pleura, and they are of a transitory nature, disappearing in 5-6 days. Similar changes have been noticed in the diaphragm, the heart, and around some of the abdominal organs. As these changes are more marked during the first 4-5 days after infection it is likely that the proteolytic secretion from the cephalic glands may be responsible for their production.

(c) Lesions produced during maturation of the worms:- As this stage in the development of the parasite is taking place inside the blood vessels of the portal system, there is very little pathology associated with it. In cases with very heavy infection however, there may be distinct changes in the surrounding liver cells. These consist mainly in a leucocytic infiltration around the blood vessels and cloudy swelling involving the adjacent liver cells. The latter is shared by the renal cortex, and is

marked probably due to general toxaemia. A congestive change has also been noticed in the spleen.

At this stage there may also be some minute haemorrhages in the mucosa of the intestines accompanied by an infiltration with polymorphonuclear, and eosinophil leucocytes.

(d) Pathology produced by mature worms:- As the worms mature they travel to the intestines and start depositing large numbers of ova therein. In experimental animals most of the ova appear to be laid in the region of the jejunum, whereas in human beings, as seen from the changes found on autopsy, the colon and the rectum appear to be most involved.

The ova are laid inside the blood vessels but they soon find their way into the surrounding tissues. Most of them are seen lying in groups in the submucosa and the mucosa, though some may be seen in the muscle coat or even under the peritoneum. Within a short time of their deposition they become surrounded by leucocytes. Faust and Meleney have noticed an increased stickiness in the outer shell which they believe to be due to a mucoid secretion, elaborated by the miracidium.

Hoeppli (1932) made extensive observations on the pathology produced by the ova S. japonicum in experimental animals. He noticed a halo of acid staining thread like structures around some of the ova in addition to the general inflammatory reaction. This was found typically in rabbits and was more

marked in certain organs e.g., the intestines and the lungs. He came to the conclusion that these threads resulted from the interaction between a secretion from the miracidia, and some substances in the surrounding tissues. This secretion appeared to be most marked around freshly passed ova, being much less around those that had been in the tissues for some time as judged from the later stages in the reaction around them. In some of the infected rabbits he gave intravenous injections of Fouadin and killed the ova. The typical reaction could not be seen around any of these dead ova.

He also noticed that the general inflammatory reaction was much more intense, and that there were more degenerative changes in the surrounding tissues in cases where this acid staining secretion was present. He is of opinion that this secretion helps the ova in their passage towards the lumen of the gut by destroying the intervening tissues.

The inflammatory lesions in the submucosa slowly enlarge and burst through the muscularis mucosae, and the mucosa into the lumen of the gut.

At this stage inflammatory changes are seen in the surrounding glands in the submucosa; some of these form cystic cavities containing purulent material. As they discharge their contents into the lumen of the gut proliferative changes are noticed in their epithelium. This, according to Faust and Meleney forms the starting point of the papillomata seen in the later stages of the disease.

About this time some changes may also be noticed in the serous coat. In the early stages infiltration around freshly passed ova side by side patches of hyperaemia with small haemorrhages here and there are seen. Later on some typical pseudo-tubercles containing ova in the centre may make their appearance. The process of repair with the

appearance of fibroblasts starts much earlier in these as compared with the lesions in the submucosa.

The characteristic thing about the lesions in the submucosa is that they discharge their contents into the lumen of the gut through minute openings, and there is no accompanying ulceration of the mucous membrane. Fibroblasts soon appear in these lesions, and the gaps in the submucosa are filled up by the formation of scar tissue. This quick repair is probably due to the fact that the ova are not capable of multiplication, and therefore the amount of toxic material is limited.

In some of these cases small abscesses have been seen, which contain haemorrhages, and are surrounded by a leucocytic infiltration, but have no ova in the centre. These are believed to be due to the action of some toxic secretions from the adult worms, most probably from the uterus of the female.

In the later stages of the disease, as seen on autopsy, in human beings, the exact pathology varies according to the amount of fresh reinfection super-imposed fresh infection. It has lost its present in each case. As most of the cases occurring in the endemic areas are exposed to infection all

the time it is quite usual to find areas of cellular infiltration around freshly passed ova side by side with extensive scarring resulting from the older lesions. The pathological changes are more marked in the colon, especially in its distal part, and the rectum.

To the naked eye there appears to be a general thickening of the large intestine. There may be matting of the omentum, and adhesions between adjacent coils of the gut. The peritoneum on its surface has lost its sheen. The thickening around the gut is most marked along the mesenteric border, and in some cases it extends to the mesentery resulting in a distinct shortening in its length. Some small nodular thickenings may also be seen under the serous coat.

On section, the most prominent change seen is the large amount of scar tissue invading all the coats of the gut. In the centre of some of these fibrous tissue masses, brownish coloured remains of degenerated eggs may be seen. Some of the eggs, which may have been deposited comparatively later may be surrounded by leucocytes, in which some fibroblasts and giant cells have made their appearance.

The submucosa appears to be increased in thickness due to extensive scarring. The mucous membrane may show some small haemorrhages, and shallow ulcerations due to the passage of ova in cases with super-imposed fresh infection. It has lost its regular appearance, and projections of variable size



SCHISTOSOMIASIS JAPONICA.
SECTION OF INTESTINE SHOWING
INVASION OF SUBMUCOSA BY OVA.
(HOUGHTON'S CASE.)

are seen extending into the lumen from its surface. In long standing cases some of these papillomata become pedunculated, and may attain a length of one centimeter or more. Structurally, they consist of a central core of submucosa, with a lining of mucous membrane on the surface. In some cases the epithelium covering these papillomata may undergo an adenomatous proliferation, and form the starting point of a malignant growth. Carcinoma of the colon or rectum often results as a complication of infection with S. japonicum.

In addition to these changes, in some sections the adult worms may be seen (singly or in copula) inside the small branches of the mesenteric veins.

The liver:- In the early stages, the eggs are lying freely in the inter-lobular veins. They may have arrived here with the blood stream from the mesenteric blood capillaries in the intestine, or may have escaped from the uteri of some of the mature female worms in the portal vessels of the liver itself. At this stage there are no pathological changes around them.

Later on these ova become surrounded by a leucocytic infiltration (mostly polymorphs or eosinophils), ultimately leading to the formation of pseudo-tubercles with the appearance of giant cells and fibroblasts, similar to those seen in the intestine. Some of these may attain the size of 1 mm. The cells in the centre of these nodules show degenerative changes.

Kupffer cells lining the blood vessels, and some large mononuclear leucocytes are seen to contain dark brown pigment granules. This pigment does not give the ferrocyanide test for haemosiderin and is not unlike the pigment (haemetin) found in the spleen in malaria as described by Brown.⁵⁴ This is evidently passed out by the adult worms. a/

In cases of infection with S. japonicum, the damage to the liver is much greater as compared with the other two species, because of the greater egg production power in this worm.

In the later stages of the disease the liver is usually enlarged, though in rare cases it may be even smaller than normal. The surface is rough and nodular. The capsule is thickened, and there may be evidence of adhesions with the parietal peritoneum, or the adjacent viscera. There may also be a thickening of the gall bladder wall.

On section there appears to be a considerable increase in the fibrous tissue. The liver cells show cloudy swelling, and fatty degeneration. In some cases the appearance is similar to interlobular cirrhosis. Faust and Meleney have described a marked thickening of the walls of the portal veins, which they believe is due to the action of toxins secreted by the adult worms. This appearance was described by Symmers⁵⁵ as "Claypipe-stem cirrhosis" in cases of infection with S. haematobium. Large numbers of typical pseudo-tubercles, some of them completely replaced by fibrous tissue, may be seen.

There may be obstruction to the portal blood flow due to extensive scarring. This produces the picture of passive congestion, resulting in enlargement of the spleen and ascites.

The spleen:- This organ is usually found greatly enlarged, especially in the later stages of the disease. This enlargement is out of all proportion to the few ova that may be seen in some cases.

In the early stages the only change seen in this organ is general congestion, with possibly a few small haemorrhages.

In the advanced case, as seen on autopsy, the capsule is thickened and may be adherent to any of the surrounding viscera. On section, the most prominent change seen is an increase in the fibrous tissue element. The trabeculae are markedly exaggerated. A few small infarcts may be seen in the cortex. The splenic corpuscles appear to be much smaller in size than normal. The blood vessel walls are thickened, and abnormally prominent. A large amount of pigment, similar to that seen in the liver, is seen inside the Kupfer cells.

It is very difficult to demonstrate the presence of ova in the spleen by examining sections, but if the softer splenic tissue is dissolved in 3 % caustic soda, they may be found comparatively easily.

⁵⁶ Perry found large numbers of ova in the spleen in cases of Egyptian splenomegaly, and other observers in Japan have confirmed this, but it is difficult to

Eosinophils are not so prominent in the lymph glands attribute the great increase in size of the organ seen as they are in the other tissues. in some cases to the changes induced by the ova only.

Later on, ova in various stages of degeneration become a constant finding; but these are not it are, the chronic passive congestion due to obstruction to the portal blood flow in the liver, and may be partially or completely replaced by fibrous thrombosis in the portal or the splenic veins.

The lungs:- The earlier lesions produced during the passage of the young schistosomuli through this organ have already been described. In the later stages some ova may find their way into the lungs and give rise to pseudo-tubercles similar to those

The urinary bladder is usually unaffected in described in the other organs; these are ultimately replaced by scar tissue, and the ova usually become calcified. To the naked eye, in cases with heavy infection, the lungs may appear like acute miliary tuberculosis, but the diagnosis can be clinched by

Snell includes appendicitis, tuberculosis, and seeing the ova on microscopic examination of the cancer amongst surgical conditions which can be sections.

The kidneys:- A certain degree of cloudy swelling in the cells of the renal cortex is always present. In heavily infected cases, actual degenerative changes may be seen in the parenchyma, as well as the convoluted tubules. These are believed to be

Schistosomiasis of the blood vessels:- Soreur due to toxæmia. In rare cases ova have also been has described the principal changes produced in the seen in the kidneys.

The mesenteric and retro-peritoneal lymph glands:- Even in the early stages of the disease venæcava are not involved. Visceral veins may show they are found to be enlarged and oedematous. The thrombosis with canalization near parts inhabited by lymphoid tissue is partly replaced by polymorphonuclear worms. In the blood vessels, the egg excites an clear and large mononuclear leucocytes.

complicated by S. japonicum.

Eosinophils are not so prominent in the lymph glands as they are in the other tissues.

Later on, ova in various stages of degeneration become a constant finding; but these are not appearance similar to syphilitic atheroma, surrounded by the usual reaction. Some of the glands may be partially or completely replaced by fibrous tissue.

The brain and the spinal cord:- Ova have sometimes been seen in these organs. They are surrounded by fibrous tissue, and there is hypertrophy of the surrounding neuroglia tissue. The urinary bladder is usually unaffected in this form of the disease. Ova have occasionally been found in other organs e.g., the heart, pancreas etc., but there is very little pathology associated with these. The earliest change seen in the bladder is a

⁵⁷ Snell includes appendicitis, tuberculosis, and cancer amongst surgical conditions which can be complicated by S. japonicum.

In cases with very heavy infection, in addition to the above described changes, there may be severe anaemia, and marked wasting. These will be discussed more fully with the clinical features of the disease.

Schistosomiasis of the blood vessels:- Sorour⁵⁸ has described the principal changes produced in the blood vessels in schistosomiasis as follows:-

Big veins e.g., the portal vein, and the venacava are not involved. Visceral veins may show thrombosis with canalization near parts inhabited by worms. In the blood vessels, the egg excites an

endothelial proliferation around itself, and there is a sub-endothelial proliferation where a spine enters the vascular coat. The latter may produce an appearance similar to syphilitic atheroma.

the urinary bladder in a man 30 years after infection

S. haematobium:- In cases of infection with this species the brunt of the disease falls on the

urinary bladder. Though occasionally cases have been described where typical terminal spined ova were seen in the faeces, and not in the urine (Dupuy⁵⁹, Nessman, and Trens⁶⁰), these are still being numbered in the curiosities of the disease. Fairley found in his experimentally infected monkeys, that the ova some times appeared in the faeces a fortnight before their appearance in the urine.

The earliest change seen in the bladder is a general congestion of the mucosa. Occasionally small,

vesicular or papular elevations may be seen on its surface, which later develop into nodular patches. These are most marked in the region of the trigone.

Microscopically large numbers of the typical terminal-spined ova are seen, especially in the submucosa. As the disease continues, there is an increase in the fibrous tissue in the walls of the bladder, till a stage may come when it has lost its elasticity and become a passive sac. This however, is fortunately rare.

A common change seen in the later stages of the disease, consists in the appearance of papillomata, of variable size, projecting from the mucous surface.

sexes. Ferguson is of opinion that the changes These are very vascular, and tend to bleed easily. produced in the ovaries by these ova may be responsible. In some cases these papillomata form the starting for sterility in some young women. Some times ova point of a cancerous growth. Fairley has described have been seen in the vermiform appendix also a case of carcinoma involving the base and neck of (Mouchet).

the urinary bladder in a man 30 years after infection with S. haematobium.

Large amounts of pigment, golden black in colour, may be seen in the interstitial tissues of the pelvic viscera. Girges⁶² has reviewed the pathology of schistosomiasis in Egypt, and is of opinion that primary

cancer in the bladder is not as common as it is described (the incidence in his experience being much less marked in this form of the disease, as compared with the Far Eastern type, but considers about $\frac{1}{2}$ %). Another interesting point he has noticed is that in cases of carcinoma of the bladder, though the possibility of the involvement of the splenic vein in the substance of the pancreas (which often metastasis are often seen in some of the distant organs e.g., the heart, and the iliac, and the retro-peritoneal lymph glands, it is rare to find contains large numbers of ova), as a probable cause of the splenomegaly seen in some cases.

Pirie has drawn attention to the frequency of secondary growths in the lumbar lymph glands.

primary hepatic carcinoma amongst the South African natives, and he regards schistosomiasis as an important etiological factor. The distal $\frac{1}{3}$ of the ureters is also involved with the bladder, and Ibrahim Aly Bey⁶³ has described several cases of stricture in these due to that condition. Out of 36 cases of stricture of the ureters, 10 were due to cicatrization of the lesions produced by the ova.

These may lead to the production of hydronephrosis, pyonephrosis, or abscess formation in the kidneys.

The ova⁶² of S. haematobium may produce in other distant organs e.g., carcinoma of the bladder, malignant growths, (carcinoma of the bladder, or epithelioma involving the penis or vulva), and rarely general peritonitis as some of the complications of this disease.

S. mansoni:—The pathology produced by this species is on similar lines to S. japonicum. The Ova have been found in almost all the pelvic earlier changes are in the intestine, especially the viscera, as well as the external genitals in both colon and rectum, and later on the liver and the

sexes. ⁶⁴Ferguson is of opinion that the changes produced in the ovaries by these ova may be responsible for sterility in some young women. Some times ova, have been seen in the vermiform appendix also, the (Mouchet).⁶⁵ area is most involved resulting in the "pipe-s. Large amounts of pigment, golden black in colour, may be seen in the interstitial tissues of the pelvic viscera. as compared with the other two, therefore. The changes in the liver and the spleen are much less marked in this form of the disease, as compared with the Far Eastern type. Day⁶⁶ considers the possibility of the involvement of the splenic vein in the substance of the pancreas (which often contains large numbers of ova), as a probable cause of the splenomegaly seen in some cases.

⁶⁷Pirie has drawn attention to the frequency of primary hepatic carcinoma amongst the South African natives, and he regards schistosomiasis as one of the important etiological factors in the production of that condition. Out of 36 cases of primary hepatic carcinoma, he found that 10 were also suffering from schistosomiasis.

The ova of S. haematobium have also been seen in other distant organs e.g., lungs, heart, brain etc., and the changes produced in these organs are similar to those discussed in connection with S. japonicum.

S. mansoni:- The pathology produced by this species is on similar lines to S. japonicum. The earlier changes are in the intestine, especially the colon and rectum, and later on the liver and the

spleen are most affected.

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whereas in cases where there are large numbers, the
peri-portal area is most involved resulting in the
"pipe-stem" type of cirrhosis.

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(1) Introduction:- An account of the symptoms produced in human beings by the schistosome worms has been compiled from the observations made by the various workers.

If untreated, the disease tends to go on for a long time, and in most cases the clinical course is modified due to reinfection from time to time in endemic areas.

For convenience of description the course of the disease may be divided into three stages:-

(1) The early stage during the invasion and maturation of the parasites.

(2) The stage of localised disease due to deposition and extrusion of ova.

(3) The late stage of tissue proliferation and repair, due to the lesions produced by the parasites and their ova.

As the signs and symptoms in stage (1) are similar in cases of infection with all the types of human schistosomiasis, they will be discussed together. Stages (2) and (3) will be described in detail in connection with S. japonicum, and the main points of difference in cases of S. haematobium, and S. mansoni will be mentioned separately.

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(1) The initial penetration of the skin by the cercariae usually causes an intense pruritus, which may be partly mechanical, and partly due to some

irritating substance excreted by the larvae. This is usually followed by a papular eruption, which has already been described in connection with the pathology produced by these worms.

Similar pruritus, and skin eruption has been described in other countries, where human schistosomiasis is unknown. Cort¹ was successful in tracing these symptoms in people who had been bathing in lake Michigan in U.S.A. to the penetration of the skin by cercariae elvae. Christenson, and Greene² found a follicular type of dermatitis in people who had been bathing in certain lakes in Minnisota, and traced it to infection with cercariae elvae from Lymnaea legnalis oppressa, and two other furcocercous cercariae. In 1928, bathers in a large artificial lake at Cardiff suffered from dermatitis. Taylor and Bayliss³ found this to be due to a cercaria closely resembling Bilharziella polonica, the adult of which is found in the mesenteric veins of ducks. In these cases however, the skin lesions disappear in 4-5 days, and as the parasites are unable to develop in the human body, there are no other symptoms.

In some cases there may be no noticeable cutaneous disturbance following exposure to infected water, and yet infection may take place as proved by the passage of the typical ova in the stools some time later. This has been specially noticed in most of the cases where the disease was contracted in the Yangtze valley, in China. Meleney⁴ has described a usually normal or subnormal in the mornings.

case where a man developed typical schistosomiasis japonica, some time after exposing himself to infected water, without having had any cutaneous disturbance. Laning⁵ makes no mention of any skin eruption in his closely observed cases on an American gun-boat on the Yangtze river.

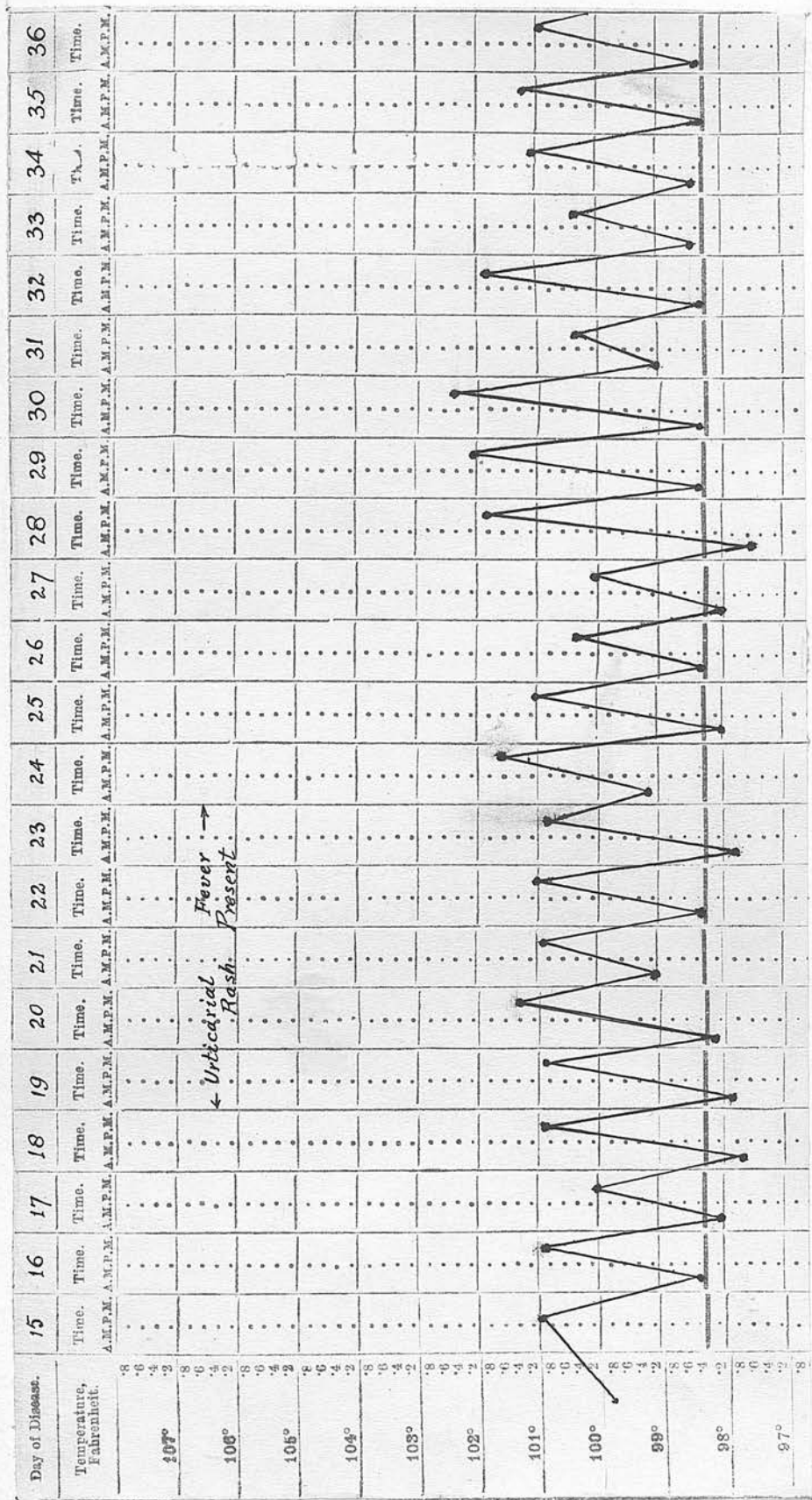
The question of incubation period of the disease is still in doubt. According to some observers e.g., Laning⁵ it would appear to be only a few days, but it is very difficult to be sure about the exact time when infection took place. Some others e.g., Lambart⁶, Faust and Meleney^{4,7} and Skinner⁸ have described a period of at least four weeks from the time of infection till the appearance of symptoms.

In cases of schistosomiasis haematobium (Fairley)⁹, and mansonii (Lawton)¹⁰, also an incubation period of 4-10 weeks has been mentioned.

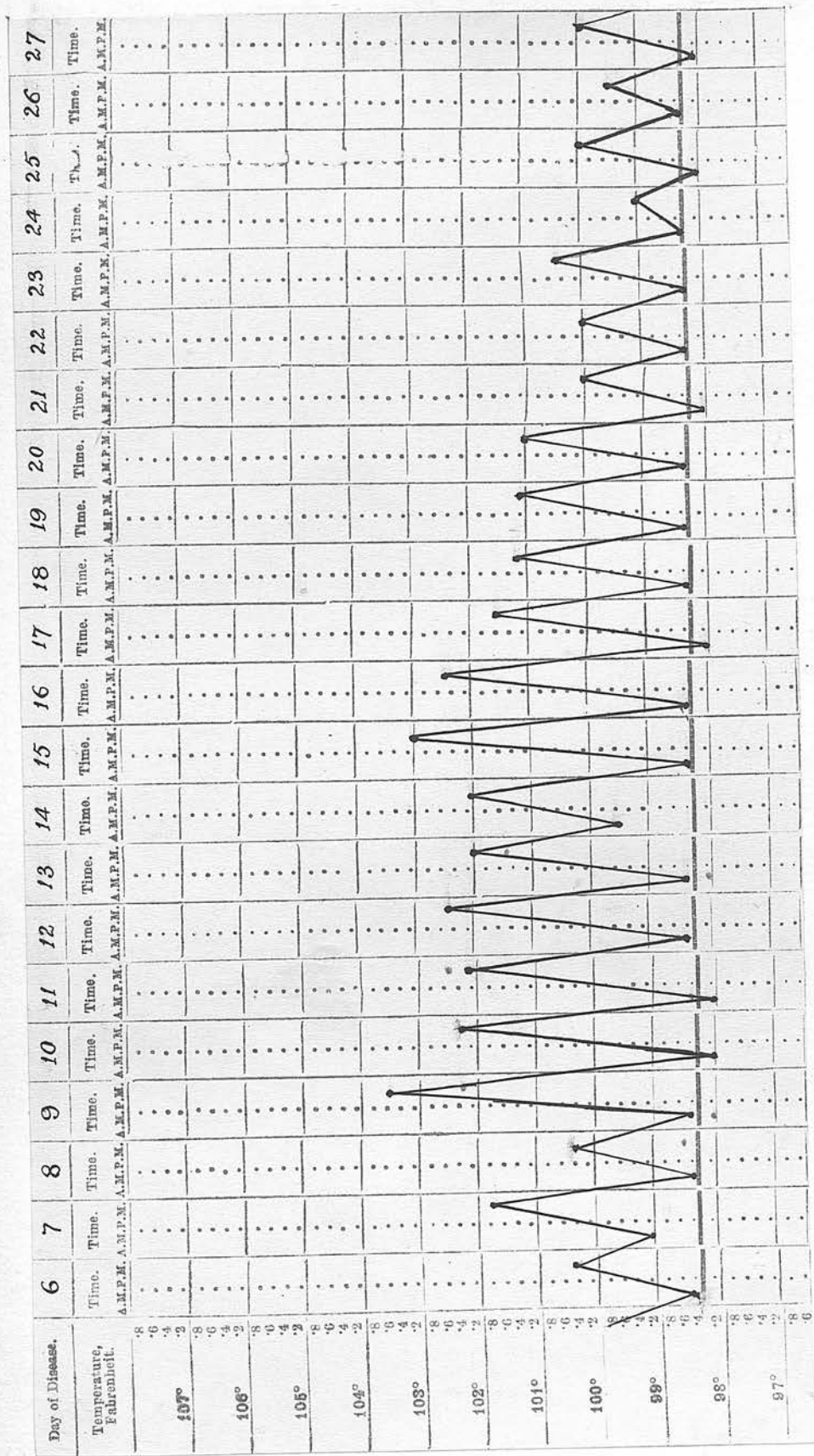
Amongst the earliest symptoms described are fever and urticaria. At this stage of the disease, these symptoms are so prominent that in the Far Eastern type of the disease, before its relationship with S. japonicum was established, it was actually given names like "Yangtze River fever", "Urticarial fever" etc.

The fever starts with general malaise and a rigor, and the temperature goes up to 102-103° F. coming down to normal some time later with profuse perspiration. This rise in temperature occurs typically in the afternoon or the evening, and it is usually normal or subnormal in the mornings. The

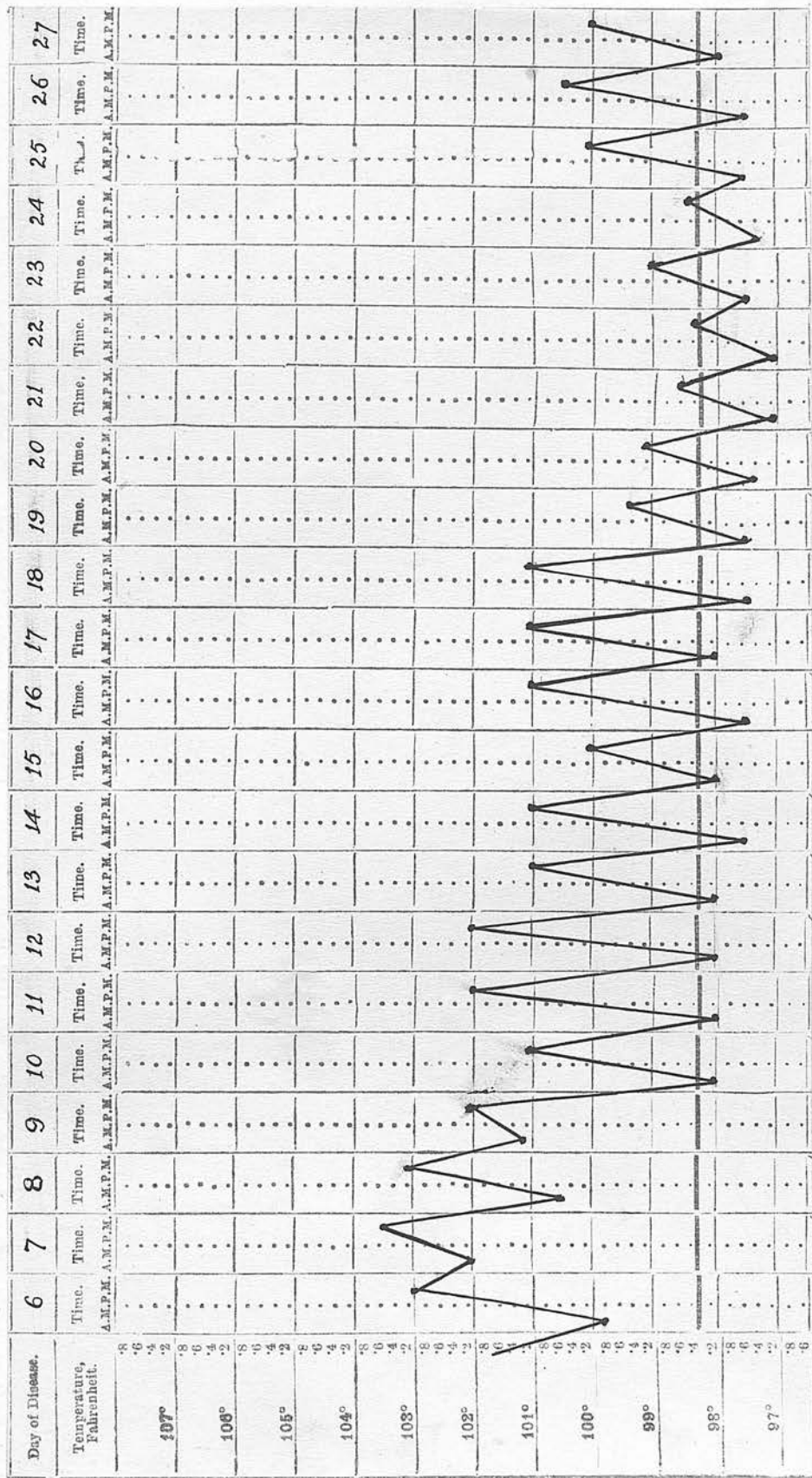
Approximate chart of a case of "Urticarial Fever", beginning about
 23 hours after infection. Arrows show the duration of the Urticarial eruption.
 (After Lambert, 1911)



Temperature chart of a case of "Urticarial Fever", beginning about
 15 days after infection. Arrows show the duration of the Urticarial eruption.
 (After Lambert, 1911)



Temperature chart of a case of *Schistosomiasis japonicum* (After Skinner)



Temperature chart of a case of *Schistogomiasis japonicum* (After Skinner)

fever is accompanied by a comparatively slow pulse. The duration of this initial period of pyrexia varies from ten days to about six weeks. Three typical temperature charts from cases of schistosomiasis japonicum are appended.

The urticaria starts about the same time as the pyrexia; it is very evanescent in character, and appears and disappears suddenly. It may first appear on any part of the body, and may spread to other parts later on. Houghton["] describes these lesions in Byam and Archibalds "The practice of medicine in the tropics" as follows:-

".....consisting at first of small, raised white areas, which rapidly enlarge, until they may measure from 3 to 4 inches (7 to 10 cm.) in diameter. The wheals may persist for an hour or two; they are white, with a pinkish areola and a central area of congestion or oedema. As they disappear the central part clears up first, the areola fading last of all, so that on examination of the patient one finds the patches in all stages of development, from the early wheal as large as sixpence to sinuous, raised, red lines, the outlines of former areas, some of which measure several inches in circumference. Dermatographia is common. The urticarial rash rarely persists longer than a fortnight and gradually disappears without leaving traces. It may invade mucous membranes in the various parts of the body, and in some cases there may be transient oedemas."

in cases of schistosomiasis japonica, are also similar

The oedema, at this stage of the disease, may in some cases be very marked. Logan¹² mentions a case in which a diagnosis of angioneurotic oedema had been made in a boy who was really suffering from schistosomiasis japonica.

Faust and Meleney⁷ believe the urticaria to be due to reaction of the human body to a foreign protein, which may be elaborated by the maturing worms or the ova. The disappearance of the urticaria a few days later may be due to cessation in the elaboration of the exact protein, or the adjustment of the host's body to its presence.

At this stage there may also be attacks of pain, some times very severe, in the back, the epigastrium, or even in the limbs. The bowels are usually irregular; short attacks of diarrhoea alternating with constipation. It is very rare to find blood in the stools at this stage.

There is also a dry troublesome cough in most cases. This may be a manifestation of the foreign protein reaction, but as transient physical signs in the lungs, suggestive of bronchitis or small patches of consolidation, have been described in most cases, it may also be due to the irritation caused by the young worms.

There is usually a slight leucocytosis, with a marked eosinophilia at this stage. The blood changes will be discussed fully at the end of this section.

The signs and symptoms, as described by Lawton¹⁰ in cases of schistosomiasis mansoni, are also similar

to these, and later on Fairley⁹ has confirmed his findings in schistosomiasis haematobium. Fairley classified his early cases as follows:-

(a) Those presenting symptoms of prolonged pyrexia and urticaria.

(b) Those with urticaria, and pyrexia of less than ten days duration.

(c) Cases with urticaria alone.

(2) The stage of localised disease:- The fever and other symptoms associated with the first stage of the disease slowly disappear within a few weeks of their onset, and are usually followed by a period of comparatively good health, varying from about three months to several years, depending on the intensity of infection, and the general resistance of the individual.

In cases of schistosomiasis japonicum, this stage is usually ushered by a second attack of pyrexia. This is less marked as compared with the first stage. The patient usually complains of a feeling of fullness in the upper abdomen, and the liver and spleen are palpable in most cases.

An almost invariable symptom in this stage of the disease consists in dysenteric attacks, alternating with periods of constipation. The stools contain blood and mucus, and their passage may be accompanied by intense griping. On microscopic examination the typical ova can be easily demonstrated. In the typical schistosomiasis stool the blood and mucus are passed after the main part of the stool,

and are therefore seen on top of the faecal mass.

The blood picture at this stage of the disease is not very constant. The red cells are usually diminished in number; they may go down to 2-3 million per cubic mm. in the heavily infected cases. The percentage of haemoglobin also falls, and the colour index always remains below unity.

The leucocytes are usually slightly increased, but as the disease advances, their number tends to fall, and there may be a severe leucopenia in some cases. The high eosinophilia usually continues through this stage.

The general health of the patient suffers considerably, and general debility and loss of weight are constant findings in most cases.

Even in untreated cases, the symptoms of this stage of the disease slowly disappear if there is no fresh infection, and there may be slight improvement in the general health, but the loss of weight usually persists.

In schistosomiasis haematobium, the clinical picture in stage (2) is centred more on the urinary system. Usually the first symptom noticed is terminal haematuria, which may or may not be associated with dysuria. There may also be other urinary disturbances e.g. urgency, and frequency of micturition due to irritation of the bladder.

The urine contains blood and mucus, and on microscopic examination, large numbers of typical terminal spined ova, pus cells, and R.B.Cs. can usually be seen.

Though In some cases there may be severe dysenteric symptoms, with the passage of terminal spined ova in the stools (O'Connor)¹³, where any of them has

The general health of the patient is usually less severely affected as compared with schistosomiasis japonica. The blood picture in this stage of the disease is similar to that described in connection with the Far Eastern type of the disease. Other symptoms may be produced due to the deposition of ova in the pelvic viscera, depending on the organ affected.

Sinderson¹⁴ has described a darkish brown pigmentation on the face extending over both cheeks, with a connecting patch over the nose giving it a butterfly type of appearance in about 20% of his cases of schistosomiasis in Baghdad.

S. mansoni:- In this species also the mature worms deposit their ova in the intestines, therefore the main signs and symptoms are similar to those described in connection with S. japonicum.

(3) The stage of tissue proliferation and repair:- Symptoms due to this stage of the disease make their appearance some years after the initial infection. These symptoms are essentially due to the gross tissue changes produced by the worms, and their ova in the various tissues and organs of the body. In cases that are diagnosed in stage (1), or even in the earlier part of stage (2), and given the proper treatment, the profound changes associated with this stage of the disease are rarely seen.

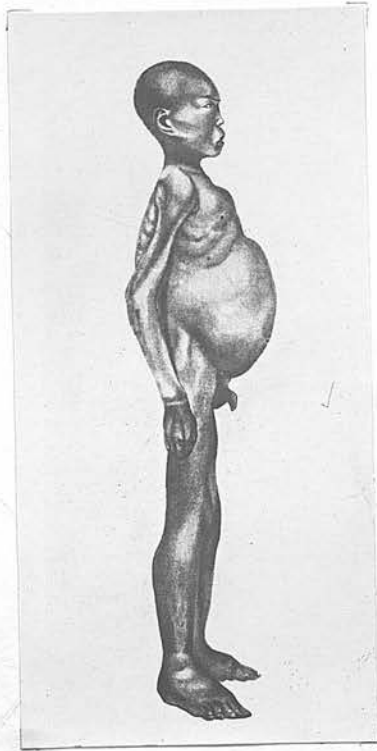
Though several cases of this disease amongst Europeans and Americans have been described, there appear to be very few cases on record, where any of them has suffered from symptoms associated with the late stages of the disease. On the other hand, the poorer people in the endemic areas in China, and Japan who usually go undiagnosed in the earlier stages of the disease, and are ever exposed to fresh reinfection suffer most heavily, and usually produce a typical picture of the late stage of tissue proliferation and repair.

The typical case in stage (3) is a pale emaciated individual, with an unduly enlarged abdomen. The facial expression is dull and tired. The eyes are usually prominent, and the conjunctiva is pale; in some cases a distinct icteric tinge may be noticeable in the sclerae.

The thorax is conical in appearance, and the ribs are very prominent. The heart is usually pushed upwards, and the beats are feeble. In some cases haemic murmurs may be heard due to the severe anaemia. The breath sounds, where not complicated due to inter-current disease are usually normal.

The abdomen is usually distended, and contains free fluid. The superficial veins are usually prominent, and the typical 'Caput medusae' may be seen around the umbilicus.

The liver and spleen are both enlarged to some degree, and in cases where the ascites is not very marked, this produces a fullness of the upper abdomen



*CASE OF ADVANCED SCHISTOSOMIASIS
IN A CHINESE BOY.*

with a distinct fissure at the level of the umbilicus, giving the abdomen the typical appearance likened by Katsurada¹⁵ to an inverted gourd.

Faust and Meleney⁷ have noticed that in a large proportion of cases, the enlargement of the liver and spleen are inversely proportional to each other, though it is by no means rare to find them both markedly enlarged. In some cases the liver may be only just palpable, and its surface may be distinctly nodular.

The colon is usually thickened and hard, and can be easily palpated through the thin abdominal wall. Rectal examination may reveal hard patches on the mucosa, and papillomata of variable size may be felt. In some cases these papillomata may be seen protruding through the anus and cause much discomfort. Unlike other types of ascites, haemorrhoids are comparatively rarely seen in these cases.

The bowels are usually irregular. Diarrhoea is quite common but the presence of blood and mucus in the stools is comparatively rare, as compared with stage (2). In some cases the typical ova may still be seen in the stools, but in the very late stages, if there has been no fresh infection, most of the worms have ceased to pass any ova, and repeated examination of the stools may fail to show any.

As the disease progresses the patient becomes very weak, and gets breathless on the slightest exertion. Marked wasting is seen in the limbs.

If the disease is contracted during early

childhood, growth and development may be considerably retarded. Faust and Meleney⁷ have described a case of a married girl, nineteen years of age who was still pre-adolescent due to having suffered from schistosomiasis japonica as a child.

Kawamura and Kassama,¹⁶ working with rabbits, found that the young ones born of mothers experimentally infected with schistosomiasis japonica, suffered from typical rickets. They were also successful in producing rickets in young rabbits, born of healthy mothers by infecting them with schistosome cercariae. They are of opinion that the toxins elaborated by the worms or their ova may affect the calcium or phosphorus metabolism.

Kiesir¹⁷ has recently described retardation in mentality physical fitness, and stamina in several school children, who were found to be infected with schistosomiasis. The children became normal again as soon as the disease was treated.

Fever, with daily rigors may also be present. This is more often seen in cases which are being reinfected from time to time.

Ozawa^{18,19} has made extensive observations on the relationship of schistosomiasis japonica with appendicitis. Out of the 42 appendices he examined, 20 contained ova of *S. ajponicum*. In 12 cases where he found ova in the appendices, the patients had not suffered from any symptoms of appendicular disease. He also observes that appendicitis is comparatively commoner in those parts of Japan, where schistosomiasis

is endemic. He concludes that the ova of S. japonicum do not induce appendicitis by themselves, but they encourage bacterial invasion.

The blood shows marked secondary anaemia; the red cells may go down to 1-2 million per cubic mm. The anaemia may be partly due to infection with other parasites e.g., hook worms, which are frequently found in these cases. The haemoglobin is very much diminished, and the colour index is usually nearer .5 than 1.

There is usually a leucopenia, but in some cases the white cells may be actually increased in number; this is usually due to secondary infection. The eosinophils are no longer as numerous as described in connection with the earlier stages of the disease; this is probably due to the fact that the worms are no longer able to elaborate the specific substances which stimulate the eosinophilia.

In some cases there may be profound jaundice due to obstruction to the bile capillaries in the liver (Skinner)²⁰.

Epileptic fits, attacks of giddiness, or paralytic symptoms may be present in some cases due to the deposition of ova in the brain or the spinal cord. Cawston²¹ mentions a case in which mental symptoms were due to the schistosome ova in the brain.

In some cases, the ova deposited in the pancreas may involve the islets of Langerhans; Day²² reports a case in which symptoms of Diabetes mellitus were due to the presence of the ova of S. mansoni in

the pancreas. Erfan²³ has recently reported a case of schistosomiasis mansoni, where the urinary sugar came down from 10 % to zero after treatment with tartar emetic; the man was on normal diet all the time.

When the disease has progressed to the stage of cirrhosis of the liver, and ascites, it is very difficult to do much for the patient. Specific medication directed against the worms is no longer able to relieve the symptoms which are due to permanent tissue changes. Death is often due to some intercurrent disease, or it may come on gradually due to progressive emaciation and debility. In some cases it may be precipitated by some complication e.g., haematemesis or cardiac failure.

Schistosomiasis haematobium:- In these cases, the general debility and emaciation are not as severe as in the case of the Far Eastern type of the disease. This stage usually supervenes in the hyper-infected individuals who are constantly exposed to reinfection.

Symptoms of chronic cystitis are present in most cases. Papillomata may be seen in the bladder on cystoscopy. The bladder wall is usually hypertrophied. The ureters are almost invariably involved in the late cases, leading to stricture and hydro-nephrosis or pyonephrosis. Urinary fistulae due to the involvement of the urethra are often responsible for producing a lot of suffering and debility. Ova may some times be deposited in the penis, leading to an elephantoid condition of the organ. The possibility of malignant growths starting in the bladder, or the

other organs has already been discussed. Large numbers of ova in the lungs may give rise to interstitial pneumonia. Pijper²⁴ found ova in the sputum in this disease. The blood picture, according to Day,²⁵ is similar to that in schistosomiasis japonica; severe secondary anaemia, with an increase in the polymorphs due to secondary infection, and a diminution in the number of eosinophils. Other organs and tissues of the body may be invaded by the ova, resulting in typical signs and symptoms. The spleen may some times be markedly enlarged in the later stages of the disease, but

S. mansoni:- In this type of the disease, the late signs and symptoms are similar to those described in connection with schistosomiasis japonica. Protracted attacks of diarrhoea are very common in this form of the disease. Another distressing symptom is the protrusion of large masses of papillomata through the anus. Induration and fistulae, in the region of the buttocks and the perineum are often seen due to infiltration with the ova. Splenomegaly with wasting, debility, and fever often dominates the clinical picture in the terminal stages. Cirrhosis of the liver, and ascites are quite common, but the anaemia is usually less severe. The blood in schistosomiasis:- Reference has already been made to the more important blood changes produced by infection with the schistosome worms in connection with the pathology, and the symptomatology of the disease.

The blood picture in the three types of human schistosomias; where uncomplicated by intercurrent disease, is similar, with minor differences which have already been mentioned.

Ozawa²⁶ made extensive observations on the blood picture of mice, experimentally infected with S. japonicum. He found that the red blood cells and the blood platelets were reduced to half the original number in five weeks after infection. The amount of haemoglobin also was proportionally reduced, and the colour index was below 1. Reticulocytes, and even erythroblasts, were seen in the early stages, but they soon disappeared. In the fully established case, the red cells appeared to be pale, but no abnormalities in their shape or size were noticed. Ozawa considers the blood picture to be suggestive of an aplastic anaemia.

Faust and Meleney⁷ examined the blood in 17 cases of schistosomiasis japonica in the various stages. The red cells in these varied from 1.5-4.4 millions; most cases having a total count of about 3 million cells per cubic mm. The haemoglobin was usually low; the colour index averaging at about .5. They also tested the fragility of the red blood cells, the bleeding time and the coagulation time in these cases, and found them to be within normal limits. The fragility of the R.B.Cs., was actually found to be decreased in most cases.

Day²⁵ is of opinion that the severity of the anaemia, and the eosinophilia in these cases, if

uncomplicated by other diseases, are directly proportional to the severity of the infection. He also found that in some cases, though the R.B.Cs, were not markedly reduced, the haemoglobin was usually very low.

The leucocytes:- In Ozawa's mice the W.B.Cs diminished for some time after infection, but there was a sudden rise again about the fifth week, as the eosinophilia appeared. After this the number slowly fell as the disease became more advanced.

In Faust and Meleney's series, the total W.B.Cs were usually less than normal, except for the cases in the ascitic stage, in whom there was a leucocytosis. This was most probably due to secondary infection.

The differential count in this disease, as described by the various observers, is usually very typical. In the early toxæmic stage, there is invariably a marked increase in the number of the eosinophils; eosinophilia of 64% (Basset-smith)²⁷ or even higher has often been reported. The eosinophilia usually persists through the stage of oviposition, but it soon disappears, if the case is cured by specific medication. In the late ascitic stage, the picture is usually dominated by polymorphonuclear leucocytes, and the eosinophils are comparatively few in number.

Girges²⁸ is of opinion, that the eosinophilia is due to a positive chemotaxic influence on the eosinophils in the circulation, produced by the toxins

Diagnosis:-

elaborated by the adult worms and their ova, and

In most cases the diagnosis of schistosomiasis these toxins also stimulate the bone marrow to is a comparatively simple matter; the presence of the greater eosinophilic activity.

characteristic ova in the dejecta being conclusive.

As these toxins disappear in the terminal The ova, if present in fair numbers are easily seen stages of the disease, due to the death of the worms with the low power of the microscope. It has however and their ova, there is a fall in the number of the to be remembered that the ova do not appear in the eosinophils. This fact is borne out by the case stools or the urine in the early stages of the disease, (No.8) in Faust and Meleney's series, where the eosinophils were only .3% no ova could be found in the due to the death of the worms. stools.

Even in stage (2), and the earlier part of The lymphocytes usually remain normal through-stage (3) they are not necessarily present in every out the course of the disease.

specimen of the dejecta that may be examined. In The total serum proteins, (especially serum view of the above fact, if one was to depend solely globulin), are found to be increased in this disease. on the examination of the dejecta for diagnosis, a These will be discussed in connection with the large number of cases would be missed. diagnosis of schistosomiasis.

The problem is often made more complex on account of certain coexisting diseases; especially due to some of the other helminths which some of the patients are suffering from.

The clinical diagnosis of schistosomiasis, in the early stage, is usually fairly easy; but in some of the cases in which the infection is not heavy enough the earlier signs and symptoms may be atypical, or too slight to attract attention. This fact is borne out by the large number of cases of schistosomiasis, that have been detected by various observers by routine examination of apparently healthy people in endemic areas.

A very important point in the diagnosis of the

early Diagnosis:-

In most cases the diagnosis of schistosomiasis is a comparatively simple matter; the presence of the characteristic ova in the dejecta being conclusive. The ova, if present in fair numbers are easily seen with the low power of the microscope. It has however to be remembered that the ova do not appear in the stools or the urine in the early stages of the disease, and in some of the late cases, they disappear again due to the death of the worms.

Even in stage (2), and the earlier part of stage (3) they are not necessarily present in every specimen of the dejecta that may be examined. In view of the above fact, if one was to depend solely on the examination of the dejecta for diagnosis, a large number of cases would be missed.

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The clinical diagnosis of schistosomiasis, in the early stage, is usually fairly easy; but in some of the cases in which the infection is not heavy enough the earlier signs and symptoms may be atypical, or too slight to attract attention. This fact is borne out by the large number of cases of schistosomiasis, that have been detected by various observers by routine examination of apparently healthy people in endemic areas.

A very important point in the diagnosis of the

early case is, the probable history of exposure to infection in an area where the disease is known to be endemic. The early papular eruption, as has already been discussed, is not a constant feature of the disease, and very few cases can be detected at this stage, because medical aid is rarely sought for what appears to be a trivial complaint.

Most cases are first seen when the pyrexia starts, and every doctor working in an endemic area, should keep the possibility of schistosomiasis in mind when treating such cases.

The temperature is usually typical, with a daily rise to about 102° F. in the evenings, coming down to normal some time later. This should call for a differential leucocyte count, when an eosinophilia may be found in positive cases. The diagnosis is more certain if the fever is accompanied by urticaria. Eosinophilia may also be present in cases of urticaria due to other causes, but the persistence of eosinophilia after the urticaria has disappeared is almost diagnostic of schistosomiasis in these cases.

In an endemic area, the typical type of fever, with urticaria and eosinophilia is usually presumptive of schistosomiasis.

Serological, and other tests, which have been devised as aids to diagnosis of schistosomiasis, especially in the early stages of the disease, will be discussed at a later stage.

With the onset of the second stage, when the ova start appearing in the faeces, or the urine, the

diagnosis becomes a comparatively easy matter in most cases. sediment is left over night, preferably in an

Erlenmeyer flask. In cases of schistosomiasis japonica, the typical eggs are found in the faeces. As the eggs, even in some of the heavily infected cases, may be passed vagariously, the examination may have to be repeated several times before they can be found. been

able to. In all cases with an enlargement of the liver or spleen, or both, and irregular dysenteric symptoms, the stools should be carefully examined for the presence of the ova. from the surface of the stool, and

shaken. If the stools contain blood and mucus, a tiny bit of mucus should be taken on a slide as a direct smear, pressed under a cover slip, and examined with the low power of a microscope. In the absence of mucus, a film should be made from the superficial part of the stool. Ringer's solution, or normal saline may be used for softening the stool if it is too hard for making a direct smear. The usual concentration methods, depending on floating the ova in hypertonic solutions, as used for the detection of other helminthic ova, are unsuitable for these, because the shell is permeable, and the ova shrink beyond recognition due to exosmosis. tags.

Ordinary. If no ova are found on examining direct smears, their presence may sometimes be demonstrated by

hatching out the miracidia. Faust and Meleney have devised a method, which consists in working the stool through a sieve to get rid of the coarser particles,

As the disease becomes more advanced, it may be possible to feel ulcers or papillomata on digital

decanting away the clear supernatant layer each time. If the sediment is left over night, preferably in an Erlenmeyer flask, the miracidia may be easily seen as minute, boat shaped organisms swimming rapidly in a straight course, with a hand lens the next morning.

Tomb and Helmy²⁹ have recently devised a sedimentation method by using which they claim to have been able to find the ova in several cases of intestinal schistosomiasis (S. mansoni), in which the results by ordinary smear examination were negative. Two c.c. of faeces are scraped from the surface of the stool, and shaken thoroughly with 30 c.c. of .7% saline. The suspension is filtered through a sieve of 100 meshes to the linear inch into a urine glass, and left to stand for some time. The sediment is examined under the microscope with a 2/3 objective. It would seem from the results quoted that this method is a great improvement over the examination of smears.

Recently Andrews³⁰ tried the various methods for finding the ova of S. japonicum in 76 cases, and found that Faust and Meleney's method of hatching out the miracidia gave by far the best results. In her 76 cases the results were as follows:-

Method.	Ova found in	Percentage.
Ordinary smear.	29.	38 %.
Sedimentation method after Tomb and Helmy.	51.	67 %.
Faust and Meleney's method of hatching out the miracidia.	76.	100 %.

As the disease becomes more advanced, it may be possible to feel ulcers or papillomata on digital

examination of the rectum. In doubtful cases, proctoscopy, or sigmoidoscopy may help by revealing the presence of papular swellings, ulcers, or papillomata on the surface of the mucous membrane. In late cases scarring may be more prominent, and in rare cases new growths may be seen. In cases with adenomata, or papillomata, a bit may be snipped off and examined microscopically for ova.

In cases where the ova are hard to find, Reed³¹ recommends that the patient be constipated for two days with opium, and then given a saline purgative. This according to him, some times reveals the ova even in cases where very few are being passed.

In stage (3), the problem of diagnosis may some times become very difficult where the ova have disappeared from the stools, and the eosinophilia is very slight or absent. Any case coming with malnutrition, anaemia, enlargement of the liver or spleen, or ascites in an endemic area should always be regarded as suspicious of schistosomiasis. The diagnosis is made more probable if the patient's work exposes him to frequent contact with infected water e.g., in boatmen, and fishermen.

Zia and Foster³³ carried out the phenoltetra-chlorophthalein test for hepatic efficiency in several cases of schistosomiasis japonica, and found definite retention of 5-30 % in all the late cases of the disease. This test, however, is of little value from the diagnostic point of view, because it is not specific in nature, and may be found positive in

other diseases which produce hepatic insufficiency. little strong nitric acid, and those that are found Useful information is often obtained in these to contain albumen are picked out. These cases, as cases by carrying out the complement fixation test well as those in which the urine contained frank with the patient's blood serum.

blood, or mucus, are subjected to systematic clinical examination till the possibility of schistosomiasis mansonii is also on similar lines, and needs no special discussion. By using this method,

though an occasional positive case may be missed, a lot of valuable time can be saved (Job).

In schistosomiasis haematobium, though the final diagnosis again rests on finding the terminal-spined ova in the urine, or rarely in the faeces, cystoscopy is some times very helpful in clearing the diagnosis in doubtful cases, when the symptomatology during stages (2), and (3) is very different. The main points in diagnosis may be summarised as follows:-

In cases with pulmonary symptoms, the ova Terminal haematuria, usually painless, in an endemic area is very suggestive. In all suspicious cases, schistosomiasis abscesses may be found on cases the urine should be examined microscopically the superficial parts of the body, and the pus in for the presence of ova. In most cases the ova can these may contain the typical ova. Boby has usually be found on examination of a centrifugalised recorded a case where terminal-spined ova were found deposit of the urine.

in the pus from an abscess over the upper eye lid in In cases with very few ova, if the patient be a young girl.

told to force out a few drops of urine in a watch glass, by straining at the end of a normal micturition, and these be examined microscopically it is diagnosis may easily be missed. Epileptic fits, possible to get a positive result.

mental changes, excessive pigmentation of the skin Albumin is almost invariably present in the (probably due to the involvement of the supra-urine in cases of schistosomiasis haematobium, renals), and several other unusual symptoms have especially while they are passing ova. This affords been described in patients suffering from this a rough and ready method for the detection of disease. Leipsoldt is of opinion, that all backward infected cases amongst large numbers of people in children in endemic areas should be examined for an endemic area. All urines are treated with a schistosomiasis.

little strong nitric acid, and those that are found to contain albumen are picked out. These cases, as well as those in which the urine contained frank

blood, or mucus, are subjected to systematic clinical

(a) The globulin reaction has been known since 1928 that schistosomiasis can be excluded. By using this method, though an occasional positive case may be missed, a lot of valuable time can be saved (Job).³⁴

Cystoscopy is some times very helpful in clearing the diagnosis in doubtful cases, when papules, pseudo-tubercles, the typical "Sandy-patches", papillomata, or new growths may be seen.

In cases with pulmonary symptoms, the ova have some times been found in the sputum. In rare cases, schistosomiasis abscesses may be found on

the superficial parts of the body, and the pus in these may contain the typical ova. Sobhy³⁵ has recorded a case where terminal-spined ova were found in the pus from an abscess over the upper eye lid in a young girl.

In some cases the symptoms may be so vague, that unless one is always on the look out, the diagnosis may easily be missed. Epileptic fits,²¹

mental changes,³⁶ excessive pigmentation of the skin (probably due to the involvement of the supra-renal), and several other unusual symptoms have been described in patients suffering from this disease. Leipoldts³⁷ is of opinion, that all backward children in endemic areas should be examined for schistosomiasis.

Serological, and skin tests also form valuable aids to diagnosis, especially in the early stages of the disease.

The diagnostic tests:-

(a) The globulin precipitation test:- It has been known since 1920 (Brahamchari)³⁸, that a flocculent white precipitate is formed by mixing the blood of kala-azar patients with distilled water. Ray³⁹ believed this to be due to incomplete haemolysis of the red cells. Later on he found that the cells haemolysed completely, if they were first washed in healthy serum. This led him to conclude, that there was some change in the serum, which prevented complete haemolysis. He found the test positive in 100 % of kala-azar cases.

Brahamchari was of opinion, that this precipitate consisted of serum globulin. Sia (1921)⁴⁰ tried the test by mixing one part of blood serum with 10 parts of distilled water, in a large number of cases; he obtained positive results in cases of kala-azar and some obscure anaemias.

Sia and Wu (1921)⁴¹, after carrying out extensive experiments came to the conclusion that Ray's idea of incomplete haemolysis was incorrect. On chemical examination, the precipitate was found to consist of serum globulin. They also found that the test was specific for kala-azar, and that in cases of that disease the total serum protein was increased; serum albumin was found to be actually decreased, but serum globulin was markedly increased.

Later on Sia (1924)⁴², tried to make the test quantitative, and devised the following method:-

20 cubic mm. of blood drawn from skin vein /
puncture of the patient are mixed with .6 c.c. of distilled water in a small tube, and a flocculent precipitate results in positive cases. Sedimentation of the precipitate in 15 minutes means :- + + + + .
Sedimentation in thrity minutes means :- + + + .
" " 45 " " :- + + .
" " one hour or longer means :- + .
If there is a haziness but no precipitate it means :- ± .

He also found that as the cases of kala-azar improved with treatment, this test became less marked, becoming negative as the patient was cured.

In 1922 Paterson⁴³ reported that the globulin precipitation test, which was hitherto regarded as specific for kala-azar, was also positive in cases of schistosomiasis, who had never suffered from kala-azar. Libby⁴⁴ also found that the test was constantly positive in cases of schistosomiasis japonica.

Faust, Meleney, and Wu,⁴⁵ carried out this test in several cases of schistosomiasis japonica, side by side with the estimation of serum proteins. They found that the test was positive in 13 out of 15 of their cases, and the serum proteins were practically equal to that in kala-azar. In 14 cases, serum globulin averaged 5.34 %, which compares favourably with the 5.31 % as estimated by Sia and Wu in cases of kala-azar. It was also found that

even in schistosomiasis, the test could be used as an index of the activity and the intensity of the infection, depending on the degree of the positive reaction. As the cases improved with specific therapy, the test became less in degree, becoming negative when the patient was cured.

This test forms a useful confirmatory procedure in the diagnosis of active cases of schistosomiasis japonica, and a valuable index of the success of treatment. In areas where schistosomiasis, and kala-azar are both endemic (e.g., in some parts of China), this test has to be interpreted with care.

(b) The serum aldehyde test:- Fox and Mackie,⁴⁶ when working on the formol-gel test as an accessory to the Wassermann test in syphilis, used some sera of kala-azar cases as controls. They found that the serum quickly became white and solid in kala-azar cases, when a drop of commercial formalin (40 % formaldehyde) was added to it. Napier⁴⁷ had found that in addition to the formation of the jelly, the serum became opaque and white. He also proved, that the opacity was due to the action of formaldehyde on the globulin fraction of the blood serum.

Fox and Mackie⁴⁶ devised a simple method for carrying out the test, in which instead of being mixed with formalin a drop of serum is taken on a slide, and exposed to the vapours of formaldehyde by inverting it on a watch glass, containing some formalin. The serum became opaque and solid in positive cases.

Faust and Meleney⁷ performed this test in 12 of their cases, of schistosomiasis japonica, and found that the results correspond roughly with their findings in the globulin precipitation test, as well as the estimation of serum globulin.

Lal⁴⁸ carried out this test in some cases of schistosomiasis haematobium, amongst Marhatta soldiers, who had contracted the disease in Baghdad. He found that Fox and Mackie's method of exposing the serum to vapours of formaldehyde was unsatisfactory. He employed Napier's original method of mixing 1 c.c. of serum with 1/17 c.c. of commercial formalin, and got positive results in some cases. His tests were not conclusive as most of the cases had been infected a long time before, and had received specific treatment.

Even in kala-azar, the test is not positive in all the cases. Napier⁴⁹ himself stated that the test becomes positive in the late stage of the disease only; usually about six months after infection.

This test is not likely to become popular in the diagnosis of schistosomiasis, because it offers no advantage over the globulin precipitation test, which is much simpler to perform and interpret.

(c) The complement-fixation test:- Yoshimoto⁵⁰ was the first to devise a complement-fixation test for schistosomiasis. He obtained his antigen by extracting fresh adult worms, from an infected calf, with absolute alcohol, and diluting the extract with three times its volume of .85 % saline. In known

positive cases, he got 100 % positive results, and in syphilis. In two groups of known cases of schistosomiasis, positive results were obtained in 88.3 % and 73 % respectively. 44 cases of syphilis, and 150 positive results in some cases who had suffered from cases suffering from other disease gave negative syphilis, even though they were free from schistosomiasis, except for one case in the latter series.

Similar extracts made from the livers of normal snails, as well as those infected with some aqueous extracts of adult worms in his experiments with the sera of experimentally infected horses. He got positive results only in horses that had been infected for a long time. He found that a positive result could usually be obtained in the early stages of the disease before the appearance of the ova in the dejecta. The test antigen from the adult worms, so he very ingeniously devised a new method of obtaining it from the livers of snails infected with the schistosome larvae. He got much better results with alcoholic extracts of these.

Fairley⁵² could not obtain a satisfactory antigen from the adult worms, so he very ingeniously devised a new method of obtaining it from the livers of snails infected with the schistosome larvae. He got much better results with alcoholic extracts of these.

He obtained his antigen from Planorbis boissyi snails infected with S. mansoni, and later on from Bullinus dybowskii snails infected with S. haematobium. The infected snail livers were macerated with absolute alcohol (at least 99.1 % by volume) 1 c.c. for each liver, at 37° c. for 24 hours, and filtered. The filtrate was evaporated at 45° c. by means of a Sprengel's exhaust pump. The residue was dissolved in .85 % saline, containing .5 % phenol (.05 Gm of the residue in 20 c.c. of the solution), and the anticomplementary dose estimated.

The general technique employed by him was the same as for the quantitative wassermann test in cases of syphilis who were free from infection with

syphilis. In two groups of known cases of schistosomiasis, positive results were obtained in 88.8 % and 73 % respectively. 44 cases of syphilis, and 150 cases suffering from other disease gave negative results, except for one case in the latter series.

Similar extracts made from the livers of normal snails, as well as those infected with some other species of schistosome cercariae gave negative results in all cases. The active principle was a

lipoid. He found that a positive result could usually be obtained in the early stages of the disease before the appearance of the ova in the dejecta. The test was found to be much more reliable in the early stages; the results in the chronic and advanced cases being unsatisfactory. He concluded that the reactive

principle Fairley regarded the value of this test as twofold:- After the dried livers had been extracted

with ab (1) As an accurate diagnostic measure in the early stages of the disease, and in latent cases.

insolub (2) As a therapeutic index for judging the effect of treatment of the disease in the adult host with various drugs; in this respect the test stands in the same relationship to schistosomiasis, as does the Wassermann test to syphilis. Is, and as such

could This work was later confirmed by Murray⁵³ in South Africa. He used antigen prepared from the livers of infected Physopsis africana snails. He

also came to the conclusion that the test was specific for schistosomiasis, and did not occur in cases of syphilis who were free from infection with

these worms.

Le Bas⁵⁴ studied the reaction carefully, and has presented evidence to show that the antigenic substances are insoluble in absolute alcohol, or acetone, and are soluble in normal saline or diluted (50 %) alcohol. She believed the active principle to be protein in nature.

Fairley⁵⁵, working with S. spindalis upheld his original idea that the active principle was a lipoidal complex, and not a protein. He showed that the residue left after evaporating the alcoholic extract did not give the reaction for proteins.

In his experiments, the antigen prepared by using alcohol of lesser strength was found to be less potent. He also concluded that the reactive principle was acetone-insoluble and alcohol-soluble. After the dried livers had been extracted with absolute alcohol, no more reactive principle could be obtained by extracting the alcohol-insoluble residue with saline or dilute alcohol.

Later on Fairley⁵⁶ found that protein-free, lipoidal, alcoholic cercarial extracts of S. spindalis could give rise to the production of anti-bodies, when injected into healthy animals, and as such could be used diagnostically. He has also worked out the changes in the anti-body titre in monkeys through the course of infection with S. spindalis.

Several observers have noticed that the complement-fixation test in schistosomiasis, is a group reaction. Fairley was able to obtain positive results in 15.

results in both S. haematobium, and S. mansoni cases with the same antigen. Cawston⁵⁷ has described a similar group reaction between the cercarial antigen from S. bovis, S. haematobium, and S. mansoni.

Hoepli (1921)⁵⁸ found that alcoholic extracts of Fasciola hepatica gave positive results with S. mansoni and S. bovis sera. Other observers e.g., Bettencourt and Berges (1922)⁵⁹, and Le Bas (1924)⁶⁰ failed to confirm his findings, though they found that the antigen appeared to be quite effective against syphilis.

Shousha⁶¹ repeated these experiments, using both alcoholic and carbolic saline extracts of F. hepatica. He concluded that "Alcoholic and watery extracts of F. hepatica possess antigenic properties against sera of Bilharziasis cases, which can be demonstrated by the complement fixation test".

"Fasciola hepatica extracts cannot be utilised for the diagnosis of F. hepatica infection in man in countries where Bilharzia is endemic."

Miyaji and Imai (1928)⁶², carried out complement fixation, and precipitin reactions in men and animals, especially in experimentally infected rabbits, and dogs. They used both alcoholic, and aqueous extracts of adult S. japonicum worms as antigen, and found the latter to be more reliable. Working with the aqueous extract antigen they got positive results in 16, out of 17 cases, who were passing ova in the stools, and in a series of 32 cases from an endemic area, where no ova could be seen in the stools, the complement was fixed in 15.

Talliaferro, Hoffman, and Cook (1928)⁶³ while working in connection with the precipitin reaction in intestinal schistosomiasis, obtained the best antigen as follows:- with S. indicum in animals, and S. Infected livers of P. guadileupensis snails, infected with S. mansonii were dried, and then extracted thoroughly in a Soxhlet apparatus, with absolute alcohol, ether, or both. The lipid free residue was then extracted with Coca's solution (containing 0.05 % Na HCO₃), the clear supernatant being used as antigen after its pH had been adjusted to 7.4-7.6. Later on they found that if infected snail livers were macerated, and then centrifugalised, most of the cercariae could be separated. These cercariae were then dried, and the antigen prepared from the resulting dry powder. This antigen was found to be more reliable than the one prepared from the snail livers. Two monkeys immunised against normal snail livers, gave positive results with antigen prepared from the infected snail livers, but negative against the antigen produced from the dried cercariae.

Fairley⁶⁴ again took up this subject in 1930 in Bombay. Working with S. spindalis, he carried out extensive serological experiments, with experimentally infected animals, as well as some human sera from cases infected with S. haematobium, and came to the following conclusions:-

(1) He found that the best antigen was prepared by extracting infected snail livers with alcohol, as

described in his earlier experiments.

(2) The group nature of these reactions was further established in obtaining positive results where the ova are not found in the dejecta, as in cases of infection with S. indicum in animals, and S. haematobium in human beings, using the antigen prepared from the livers of P. exustus snails infected with S. spindalis.

(3) Practically all the experimentally infected goats gave positive results. The titre showed a primary rise during the second week after infection, due to the cercarial invasion, and a secondary rise about the 5-9th week related to portal thrombi containing the adult worms.

(4) Some of the infected animals were treated with urea-stibamine, tartar emetic, or emetine hydrochloride, and though the reaction always became weak after this, negative results could be obtained in a few of the animals only. Low grade positive reactions were found to persist in some animals for several weeks, after all living worms had disappeared.

(5) Consistently negative results were obtained in a larger number of tests with non-schistosome sera, but syphilitic sera still gave positive results in 50 % of their cases; these were not obtained when the antigen prepared from the dry cercarial powder was used.

(6) In cases where the blood was strongly positive, similar results could be obtained with antigen produced from normal snail livers pleural, peritoneal, or pericardial fluids.

It may be concluded from the above that, though there still appears to be considerable difference of opinion in connection with the results obtained by the various observers, by using different methods complement fixation test in the diagnosis of schisto-

for preparing the antigen, the value of the test in the diagnosis of schistosomiasis, especially in cases where the ova are not found in the dejecta, is certain. The test, as originally stated by Fairley, is also useful in estimating the effect of specific drug therapy. A weak positive may be obtained for some time after all the worms have been successfully killed; this may be due to the dead worms in the body.

(d) The precipitin test:- Several observers e.g., Miyaji and Imai (1928)⁶², and Taliaferro, Hoffmann, and Cook (1928)⁶³ have tried to elaborate a precipitin test in schistosomiasis, due to its comparative simplicity, as compared with the complement fixation test. Miyaji and Imai were able to obtain positive results in only 50 % of their known cases of schistosomiasis japonicum.

Taliaferro, Hoffman, and Cook, working with their antigen (already described) prepared from dried infected snails obtained satisfactory results with schistosome sera, but syphilitic sera still gave positive results in 50 % of their cases; these were not obtained when the antigen prepared from the dry cercarial powder was used.

Antigen produced from normal snail livers was found to give consistently negative results with schistosome sera.

These results are certainly very encouraging, but whether this test will be able to replace the complement fixation test in the diagnosis of schisto-

somiasis, remains to be seen.

(e) Skin test in schistosomiasis:- Fairley and Williams (1927)⁶⁵ devised an intra-dermal test for this disease. They found that if an antigen obtained from dried snail livers infected with S. spindalis was injected into the skin in cases of schistosomiasis a typical reaction could be obtained. In some cases a wheal, surrounded by a zone of congestion appeared rapidly at the site of the injection, where as in others it appeared 3-24 hours later constituting a delayed response. They got positive results in 7 out of 8 known cases of schistosomiasis haematobium, three giving a delayed result.

They consider the test to be of diagnostic value only, because two serologically cured cases, still gave a positive result. This test should prove useful as a quick method for the diagnosis of schistosomiasis, especially where a large number of people may have to be examined.

These experiments were repeated by Manson Bahr⁶⁶ in 1929. He also found that the test remained positive in two cases after treatment with 20, and 21 grains of sodium antimony tartrate.

Fairley's antigen was found unsuitable for skin tests by Khalil and A. Hassan⁶⁷ in the Research Institute, Cairo, owing to the fact that uninfected snail liver extracts also gave a positive reaction in a certain number of normal people. Better results were obtained with an antigen prepared from adult *Schistosoma bovis* worms from cattle. Forty-two

persons who were definitely known to be free from schistosomiasis gave negative results, and out of 132 known cases, 128 gave immediate positive, and another two a delayed reaction after 24 hours.

in exc Differential diagnosis of schistosomiasis:—*cal*

caloul The early toxæmic stage of the disease, when the symptoms first appear, is often mistaken for other febrile conditions, e.g., the enteric *ay* group of fevers, malaria, kala-azar, or acute *known to* miliary tuberculosis. The diagnosis is usually *The* made on finding a slow pulse, and a marked eosinophilia; the complement-fixation test, or where kala-azar can be excluded, the globulin precipitation test may help to make the position clear. *ave to*

be excl In cases where the lung symptoms are more *these* prominent, bronchitis, or broncho-pneumonia may *d* have to be excluded. *is may some times be very difficult.*

Thorough Cases with urticaria, and oedema have to be distinguished from fish or food poisoning, and *t may* rarely angio-neurotic oedema. The pain in the epigastrium may suggest liver abscess; this may be *ble* excluded due to the absence of amoebic cysts in the stools, and a polymorphonuclear leucocytosis. *infor-*

mation In all these cases the diagnosis is finally established on finding the typical ova in the dejecta.

In the second stage, the intestinal schistosomiasis (both japonicum and mansoni) present a picture very similar to other types of dysentery, but the *can* diagnosis is usually fairly easy in most cases, the typical ova being found on microscopic examination of the stools.

In urinary schistosomiasis, the febrile cases may some times be confused with acute nephritis; here again the careful examination of the urine and blood would help. Care has to be taken in excluding other causes of haematuria e.g., vesical calculi, papillomata etc., which are often associated with the disease.

Chyluria, due to filariasis bancrofti, may some times have to be excluded; it has been known to coexist with schistosomiasis in the same case. The diagnosis is made by finding the microfilariae in the blood at night.

In the late stages of the disease, malarial cachexia, splenic anaemia, or kala-azar may have to be excluded. As the prominent symptoms in all these consist of a secondary anaemia, with an enlarged spleen, the diagnosis may some times be very difficult. Thorough examination of the blood and stools may help in some cases, and the complement-fixation test may clear the diagnosis in some doubtful cases.

Some of the late cases may closely resemble alcoholic, or syphilitic cirrhosis of the liver, or tuberculous peritonitis; in these cases useful information is some times obtained by going into the past history of the case.

Infection with other helminths, especially ankylostomiasis, which are accompanied by anaemia, eosinophilia, and gastro-intestinal disturbances can usually be excluded by finding the offending worms, or their ova in the stools.

The diagnostic tests carried out in Bombay:-

again Introduction:- Thirty cases suffering from obscure dysenteric symptoms, anaemias, or ascites were selected in the King Edward VII Memorial Hospital, Bombay, during the period November 1933 to May 1934, and carefully examined for infection with S. japonicum. Their stools were examined both by the direct smear method, and by trying to hatch out the miracidia (vide infra).

Routine blood examination was also carried out in each case, paying special attention to the differential leucocyte count.

(A) The stools:- Smears from fresh specimens of the stools were made (in .85% saline if the faeces were hard), and examined with the 2/3 rd. objective of the microscope; at least three films being examined in each case.

In some cases, where amoebiasis was suspected, smears were also made in iodine solution to facilitate the identification of the species. The parasites found in the stools in each case were noted.

An attempt was also made to hatch out the miracidia by employing a slight modification of the method advocated by Faust and Meleney.

The specimen of the stool was shaken up with about 1,000 c.c. of tap water in a large sized flask till it was completely emulsified, and then left undisturbed for about half an hour. The supernatant fluid was then decanted off, and fresh tap water was added to the sediment. This was again shaken and

left to stand for some time, the supernatant fluid again replaced by tap water. This process was repeated 4-5 times till the supernatant fluid remained clear on standing. It was then left undisturbed for about 24 hours at ordinary room temperature (about 25-30°C.). The upper layers of the supernatant were carefully examined, with a hand lens, for the possible presence of miracidia the next morning. The results of these investigations are shown in Table I.

(B) The blood:- The blood counts were carried out with a Neubauer counting chamber, and the same red, and white blood cell pippets were used in all these cases. For haemoglobin estimation a Sahli haemoglobinometer was employed.

For the differential leucocyte counts 200 white blood corpuscles were counted in each case. Table II shows the results of these blood studies.

It will be seen from a perusal of Tables I, and II that no evidence of possible schistosomiasis was found in any of the thirty cases examined.

Case No.	Hospital No.	Sex	Age	Principal Disease
1	H 209	F	40	Anaemia
2	H 311	M	15	Anaemia
3	H 303	M	25	Dysentery
4	H 1095	M	40	Anaemia
5	H 1322	M	20	Chronic
6	H 1324	M	50	Anaemia
7	H 1325	M	35	Severe Anaemia
8	H 1326	M	20	Chronic
9	H 1327	M	40	Anaemia
10	H 1328	M	30	Severe Anaemia
11	H 1329	M	20	Chronic
12	H 1330	M	20	Anaemia
13	H 1331	M	20	Anaemia
14	H 1332	F	45	Severe
15	H 1333	M	25	Dysentery

TABLE I
Results of stool examination of 30 cases from the K.E.M. Hospital, Bombay.

Case No.	Hospital No.	Sex	Age	Principal Symptoms	Ova of					Amoebae or cysts		Miracidia of <i>S. japonicum</i>
					<i>S. jap.</i>	<i>Ancylostoma</i>	<i>Ascaris</i>	<i>Taenia</i>	<i>Trichuris</i>	<i>E. histolytica</i>	<i>E. coli</i>	
1.	H 209	F	40	Anaemia, Diarrhoea	0	+	0	0	+	0	+ cysts	0
2.	H 311	M	15	Anaemia	0	0	+	0	0	0	0	0
3.	H 505	M	25	Dysentery	0	0	0	0	++	0	0	0
4.	H 1093	M	40	Anaemia, Diarrhoea	0	+	0	0	+	0	0	0
5.	H 1322	M	20	Chronic dysentery	0	0	0	0	++	+	++	0
6.	H 1584	M	50	Anaemia	0	0	0	0	0	0	0	0
7.	H 1909	M	45	Severe Anaemia	0	+	0	0	+	0	0	0
8.	H 1917	M	18	Chronic Diarrhoea	0	++	0	0	0	0	0	0
9.	H 1924	M	40	Ascites	0	0	0	0	+	0	0	0
10.	H 2119	F	35	Severe Anaemia	0	0	++	0	++	0	0	0
11.	H 2503	M	20	Anaemia	0	0	0	0	0	0	0	0
12.	H 2623	F	20	Anaemia, Diarrhoea	0	0	0	0	+	0	0	0
13.	H 2720	F	45	Severe Anaemia	0	0	0	0	++	0	0	0
14.	H 2928	M	26	Dysentery	0	0	0	0	0	++	+	0

Case No.	Hospital No.	Sex	Age	Principal Symptoms	Ova of					Amoebae or cysts		Miracidia of <i>S. japonicum</i>
					<i>S. jap</i>	<i>Ancylostoma</i>	<i>Ascaris</i>	<i>Taenia</i>	<i>Trichuris</i>	<i>E. histolytica</i>	<i>E. coli</i>	
15.	H 2935	F	30	Anaemia	0	0	0	0	0	0	0	0
16.	H 3150	M	39	Chronic Dysentery	0	0	0	0	+	0	0	0
17.	H 3151	F	-	Anaemia, Diarrhoea	0	0	+	0	++	0	0	0
18.	G 9094	F	8	Anaemia	0	0	+	0	0	0	0	0
19.	G 9100	M	40	Anaemia	0	0	0	0	+	0	0	0
20.	G 9104	F	30	Severe Anaemia	0	0	0	0	0	0	0	0
21.	G 9393	M	37	Anaemia, Diarrhoea	0	0	0	0	+	0	0	0
22.	G 9449	M	23	Dysentery	0	0	0	0	0	+	++	0
23.	G 9494	M	25	Anaemia, Dysentery	0	0	0	0	++	0	0	0
24.	G 9504	M	18	Anaemia, Diarrhoea	0	++	0	0	0	0	0	0
25.	G 9683	M	12	Severe Anaemia	0	0	0	0	++	0	0	0
26.	G 9690	F	26	Anaemia	0	0	0	0	0	0	0	0
27.	G 10090	M	28	Anaemia, Diarrhoea	0	0	0	0	0	0	0	0
28.	G 10269	F	23	Chronic Dysentery	0	+	0	0	++	+	0	0
29.	G 10265	F	45	Anaemia	0	+	0	0	0	0	0	0
30.	G 10431	M	21	Dysentery	0	0	0	0	+	0	0	0

TABLE II
Blood studies on 30 cases from the K.E.M. Hospital, Bombay.

Serial No.	Hospital No.	Sex	Age	Million R.B.C.	Hæmoglobin %	Colour index	Leucocytes				Abnormal Blood cells
							Total Thousand	Polymorphs %	Lymphocytes %	Eosinophiles %	
1.	H 1209	F	40	3.6	50	.69	7.5	72	23	5	-
2.	H 311	M	15	3.7	35	.47	4.7	62	32	4	Anisocytosis
3.	H 505	M	25	4.5	57	.63	9.2	60	25	9	-
4.	H 1093	M	40	1.5	30	1.00	5.3	72	24	3	-
5.	H 1322	M	20	4.3	52	.60	7.1	65	24	4	-
6.	H 1584	M	50	3.2	75	1.10	5.2	45	36	3	Normoblasts
7.	H 1909	M	45	1.9	32	.89	6.3	65	28	2	Megalocytes
8.	H 1917	M	18	3.8	53	.70	7.5	62	31	1	-
9.	H 1924	M	40	3.1	45	.70	13.2	80	16	2	-
10.	H 2119	F	35	1.8	32	.89	5.0	56	42	1	Anisocytosis & Normoblasts
11.	H 2503	M	20	1.9	30	.80	4.6	54	42	3	-
12.	H 2623	F	20	4.0	70	.87	4.5	58	36	1	-
13.	H 2720	F	45	1.2	23	.96	4.8	62	35	1	-
14.	H 2928	M	26	4.2	58	.69	9.2	75	21	3	-

Serial No	Hospital No	Sex	Age	Million R.B.C.	Hæmoglobin %	Colour Index	Leucocytes				Abnormal Blood cells
							Total Thousand	Polymorphs %	Lymphocytes %	Eosino- philes %	
15.	H 2935	F	30	1.8	34	.94	6.3	55	37	6	-
16.	H 3150	M	39	3.8	52	.68	7.5	63	30	2	-
17.	H 3151	F	-	2.6	48	.92	5.1	58	28	9	-
18.	G 9094	F	8	3.7	42	.56	10.3	78	14	2	-
19.	G 9100	M	40	4.0	46	.57	4.8	68	24	5	-
20.	G 9104	F	30	2.8	28	.50	3.0	78	20	0	Poikilocytosis
21.	G 9393	M	37	2.2	46	1.00	4.6	67	28	4	- do -
22.	G 9449	M	23	3.4	32	.47	9.1	66	20	12	-
23.	G 9494	M	25	3.4	45	.66	5.6	64	28	2	-
24.	G 9504	M	18	2.4	35	.73	4.8	68	29	3	-
25.	G 9683	M	12	2.1	23	.54	5.8	62	35	1	Poikilocytosis
26.	G 9690	F	26	2.0	35	.87	7.2	58	34	4	-
27.	G 10090	M	28	1.8	32	.89	4.9	55	39	2	-
28.	G 10269	F	23	3.4	64	.94	7.6	68	26	5	-
29.	G 10265	F	45	3.6	48	.67	6.5	62	32	4	-
30.	G 10431	M	21	3.8	42	.55	9.2	58	36	2	-

Serological tests:-

These were carried out according to the method advocated by Fairley (1930).

The antigen, which was kindly supplied by Dr. Soparker of the Haffkine institute, Bombay, had been prepared from the livers of the snails (I. exustus) infected with Schistosoma spindalis, as follows:-

Snails were collected from the fresh water tanks, and ponds, and put in test tubes, one snail in each, containing 4-5 c.c. of tap water. These were then left at ordinary room temperature for 24 hours, and examined for the presence of the cercariae of S. spindalis with a hand lens, or in case of doubt under the microscope.

The snails which were definitely found to be infected with S. spindalis were dissected, and the livers, or the digestive glands teased out with mounted needles. Each was examined microscopically, and those found heavily infected were separated, and placed in a vessel containing absolute alcohol, 1 c.c. for each liver.

After shaking for 20 minutes, the mixture was extracted for 24 hours at 37° C., thoroughly shaken again, and run through a filter paper. The clear yellow filtrate was concentrated in a water bath at $40-45^{\circ}$ C. by bubbling air through the solution by means of an exhaust pump, till it became turbid. Enough alcohol was then added to clarify the solution, and this concentrated extract was stored in an ice chest till required, when it was diluted with the appropriate amount of normal saline.

1 in 5 A 2% suspension of well washed sheep's red blood corpuscles, sensitized with 2 M.H.D. of anti-sheep haemolysin of a titre exceeding 1 in 5,000 was employed in the tests.

The complement:- Serum was obtained from pooled blood of (at least three) guinae pigs, and titrated as follows:- serum, and in row III, each tube contained

two volumes of guinae pig serum in normal saline in the strengths of 1 in 10, 20, 30, 40, 50, 60, 70, and 80 were mixed with one volume each of the 2% suspension of sheep's red corpuscles, and 3 volumes of .85% saline. These were then incubated for one hour. The M.H.D. of the complement was estimated from the tube containing the smallest amount of the complement which had produced complete haemolysis. Best results were obtained in the tests proper by using 3, $4\frac{1}{2}$, and 6 M.H.D. of complement.

III For the actual tests, the serum obtained from the blood of the suspected cases was decomplemented by heating for 15 minutes at 55° C. on the day on which the test was performed. The serum was diluted 1 in 5 with .85% saline. the complement in the presence of normal serum. The titre of the antigen was determined by finding the upper limit of the antigenic dilution, which in unit volume, deviated 3 M.H.D. of complement in the presence of unit volume of a 1 in 5 dilution of a known Bilharzia serum, obtained from a patient who had been passing ova of S. haematobium in his urine.

Three rows of 8 tubes each were taken. The tubes in row I contained:- 1 volume (0.1 c.c.) of

1 in 5 Bilharzia serum, one volume of .85% saline, one Row I. 0.1 c.c. of antigen 0.1 c.c. of the patient's volume containing 3 M.H.D., and one volume of an serum 0.1 c.c. of complement (containing 3 M.H.D.) 0.1 ascending series of antigen in the dilutions 1 in 5 c.c. of .85% saline. to 1 in 200.

Row II. Same as in row I, except complement 0.15 c.c.,

In row II one volume of a de complemented serum and saline .05 c.c.

from a normal man was used instead of the known

Row III. Same as in row I, except complement .2 c.c.,

Bilharzia serum, and in row III, each tube contained and no saline.

two volumes of .85% saline, with one volume each of

Row IV. 0.1 c.c. of the patient's serum 0.1 c.c. of the the complement, and the ascending series of antigen. complement 0.2 c.c. saline.

These were incubated for one hour at 37° C.,

These were incubated for one hour at 37° C., and

and then one volume of a 2% suspension of sensitized

then 0.1 c.c. of a 2% suspension of sensitized sheep's

sheep's corpuscles was added to each tube. Readings

red corpuscles was added to each tube. The usual controls

were made after incubating for an other hour. The

also were employed. Row IV acts as a control against any

results were:-

anticomplementary tendency in the particular serum under

Row. Serum. Dilution of antigen, 1 in investigation. Readings 5 10 20 40 60 80 100 200 were

I Bilharzia.

haemolysed. One control of a known Wasserman positive

II Normal. 0 0 0 0 0 0 0 0

serum was also employed with each batch.

III Nil. 0 0 0 0 0 0 0 0

Results:- The final readings were interpreted as

This indicated that the extract was satisfactory follows:-

for serological work. There was no haemolytic tendency,

No haemolysis in tubes in the rows I, II, and III

the anti-complementary dose was less than 1 in 5, and it

means that at least 6 M.H.D. of complement have been

did not fix the complement in the presence of normal

fixed, and this is marked:- + + +.

serum. Bilharzia serum gave positive results uptill a

No haemolysis in tubes in rows I, and II means

dilution of 1 in 200.

that 4 M.H.D. of the complement have been fixed, + +.

The antigen was tested against 4 known cases of

No haemolysis in tubes in row I means that 3 M.H.D.

syphilis (Wasserman strongly positive), and gave negative

of complement have been fixed, +.

results. In the following tests a 1 in 40 dilution of

Incomplete haemolysis is marked ±.

the antigen was employed.

25 cases from the King Edward VII Memorial Hospital

The routine test:- Racks containing 4 rows of

Panel, and 11 Fishermen from Dharavi (near Sion, C.I.P. Ry.)

tubes were used.

Row I. 0.1 c.c. of antigen 0.1 c.c. of the patient's serum 0.1 c.c. of complement (containing 3 M.H.D.) 0.1 c.c. of .85% saline.

Row II. Same as in row I, except complement 0.15 c.c., and saline .05 c.c.

Row III. Same as in row I, except complement .2 c.c., and no saline.

Row IV. 0.1 c.c. of the patient's serum 0.1 c.c. of the complement 0.2 c.c. saline.

These were incubated for one hour at 37° C., and then 0.1 c.c. of a 2% suspension of sensitized sheep's red corpuscles was added to each tube. The usual controls also were employed. Row IV acts as a control against any anticomplementary tendency in the particular serum under investigation. Readings were made when all controls were haemolysed. One control of a known Wasserman positive serum was also employed with each batch.

Results:- The final readings were interpreted as follows:-

No haemolysis in tubes in the rows I, II, and III means that at least 6 M.H.D. of complement have been fixed, and this is marked:- + + +.

No haemolysis in tubes in rows I, and II means that 4½ M.H.D. of the complement have been fixed, ++.

No haemolysis in tubes in row I means that 3 M.H.D. of complement have been fixed, +.

Incomplete haemolysis is marked ±.

26 cases from the King Edward VII Memorial Hospital Parel, and 11 fishermen from Dharavi (near Sion, G.I.P.Ry.)

Prognosis of schistosomiasis:
 were examined serologically, by the above method, and
 The prognosis in this group of disease depends
 gave consistently negative results.

mainly on the intensity of the original infection.

As has already been stated, these worms are incapable
 of multiplication inside the body of the adult host,
 therefore the damage that may be expected in each
 case depends solely on the number of cercariae which
 penetrate the skin.

Other important factors in the prognosis are
 the possibility of reinfection, and the time when
 specific treatment is administered. In people who are
 infected with a single dose of cercariae, and then
 removed from the endemic area, the symptoms are
 rarely severe, and very little permanent damage is
 done to the viscera. Much stress is placed on the
 importance of early treatment, and the prevention of
 reinfection as two of the most important points from
 the prognostic point of view.

Several cases have been reported on the long-
 evity of the disease. Kirkland²² made a
 study of 486 cases reported during the South African
 war, and concluded that schistosomiasis was a very
 prolonged disease, lasting for as long as thirteen
 years. He found that the mortality rate amongst
 Europeans, removed from the endemic area did not
 exceed 1%. Gaxton has recorded a case where live
 ova were being passed in the urine, 45 years after
 the original infection; in this case the question of
 reinfection could not arise, because he had been away
 from the endemic area. Kirkland mentions a case

Prognosis of schistosomiasis:-- The prognosis in this group of diseases depends mainly on the intensity of the original infection. As has already been stated, these worms are incapable of multiplication inside the body of the adult host, therefore the damage that may be expected in each case depends solely on the number of cercariae which penetrate the skin. in an endemic area also depends on the Other important factors in the prognosis are the possibility of reinfection, and the time when specific treatment is commenced. In people who are infected with a single dose of cercariae, and then removed from the endemic area, the symptoms are rarely severe, and very little permanent damage is done to the tissues. Girges⁶⁸ lays stress on the importance of early treatment, and the prevention of reinfection as two of the most important points from the prognostic point of view. Lambrey and Coleman found Several observers have commented on the longevity of the schistosome worms. Harrison⁶⁹ made a study of 466 cases infected during the South African war, and concluded that schistosomiasis was a very prolonged disease, lasting for as long as thirteen years. He found that the mortality rate amongst Europeans, removed from the endemic area did not exceed 1%. Cawston has recorded a case where live ova were being passed in the urine, 28 years after the original infection; in this case the question of reinfection could not arise, because he had been away from the endemic area. Kirkland³⁶ mentions a case

where a soldier was passing ova in his urine in 1927, when the disease had been contracted in 1902.

~~adequa~~ In the typical hyperinfected cases seen in China and Egypt (due to frequent reinfection), a considerable amount of debility and suffering is produced, and the death rate directly or indirectly due to this disease is much higher.

The prognosis in an endemic area also depends on the percentage of the population infected. In areas where large numbers of people are infected, there is usually a greater number of snails infected leading to the production of more cercariae, resulting in more numerous, and heavily infected cases.

The prognosis is most favourable in cases who are diagnosed in stage (1), or the early part of stage (2), and given adequate treatment, especially if risk of reinfection can be avoided by removing them from the endemic area. Lanbrey and Coleman found the mortality rate in a large number of cases, treated by them to be under a half percent.

As the tissue changes produced by the worms, in stage (3) are permanent, specific therapy is of little avail, and the prognosis in these cases is not so good. According to Girges the life of the case with ascites is limited to about two years.

The problem of prognosis of schistosomiasis, in an endemic area, is closely linked up with that of prophylaxis. The most important points, in saving a community from the ravages of this disease consist

in the timely diagnosis and treatment of the infected cases, and the prevention of fresh infection by

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The treatment of schistosomiasis:-

Introduction:- The treatment of schistosomiasis resolves itself into (a) Specific therapy, as directed against the adult worms and their ova, in the body of the definitive host; and (b) Symptomatic treatment.

(a) **Specific therapy:-** The ideal drug for this purpose would be one, which can kill the parasites in vivo in concentrations which are harmless to the host. Several workers had been in search of such a drug, and some of them had a certain measure of success with some medicines, but none of these could be relied upon to destroy all the parasites. In China and Japan, Quinine was given extensive trial, and though it gave some relief in the earlier stages of the disease, it failed to make the eggs disappear entirely from the stools (Miyagawa)¹.

Arsphenamin was tried in China and Egypt without apparent effect.

Schistosomiasis was considered an incurable disease, with a mortality of over 90 % until the advent of antimony therapy. McDonagh² was the first to mention the use of antimony as a specific in this disease. He claims to have treated his first case of schistosomiasis with tartar emetic in 1911, and commented on this drug as a cure for the disease in his book "Biology and treatment of venereal diseases" published in 1915³. In 1918 he discussed the comparative merits of three preparations of antimony which he had tried. He found that both antiluetic (antimony potassium ammonium tartrate),

and colloidal antimony (antimony sulphide) were better than tartar emetic. Colloidal antimony was the least toxic, but antilueticin was found to be most potent.

In a later communication (1920)⁴, after a more extensive trial of these preparations, he concluded that tartar emetic was the most useful compound. He found that arsenobenzene was useless in the treatment of schistosomiasis.

In the mean time Christopherson had started using tartar emetic independently in the treatment of schistosomiasis in May, 1917 at the Khartoum civil hospital, and it was after the publication of his successful results⁵ that the drug became better known.

He claimed that if given with due care, tartar emetic could destroy all worms and their ova without harming the host. Several other observers confirmed Christopherson's findings, and lately the drug has been tried in the Far East also with satisfactory results. In spite of the fact that toxic symptoms, both immediate or delayed, are often produced in some of the cases, this drug has been used extensively in the various countries where schistosomiasis is endemic.

The search for a more potent drug, with less danger of toxic symptoms in the host, was continued, and several other preparations of antimony were tried. These will be discussed at a later stage.

Besides antimony, emetine hydrochloride appears to be the only other drug which has given good

results. Though not as potent as tartar emetic, it has the advantage that it can be given subcutaneously or intra-muscularly, and is very useful in some cases, where for one reason or another tartar emetic is contra-indicated. It has the further advantage of ridding the patient of certain other parasites e.g., Entamoeba histolytica, which may be coexisting with the schistosome worms.

Though excellent results have been claimed for some of the other preparations that have been tried, they have all got their drawbacks, and the search for the ideal drug still continues.

Specific therapy can only be useful in the early stages of the disease. In the late stage with permanent damage to the tissues, symptomatic treatment and surgery may give relief from the more urgent symptoms.

Antimony preparations:-

(1) Tartar emetic (Antimony potassium tartrate):- Since the advent of this drug it has been estimated that 80 % of the cases of schistosomiasis can be cured.⁶

Tartar emetic is obtainable in the form of colourless crystals, with triangular facets; on exposure to air they turn white and opaque. It is soluble in water (1 in 12), but insoluble in alcohol. In water it forms a slightly acid solution (pH 4.5), and is unstable at the pH of the body tissues. Its chemical formula is $2(\text{KSbO}_3 \cdot \text{C}_4\text{H}_4\text{O}_6) \cdot \text{H}_2\text{O}$.

course is complete.

The route of administration:- The choice of the route of administration in the case of tartar emetic is limited to intravenous injection. When given by the mouth the drug acts as a powerful emetic, even in very small doses; the pharmacopeal dose being $\frac{1}{8}$ gr. as an expectorant, and $\frac{1}{2}$ gr. as an emetic. In larger doses it acts as a severe irritant of the gastro-intestinal system, and produces symptoms similar to acute arsenical poisoning.

It cannot be given by subcutaneous or intramuscular injection, because it produces necrosis of the tissues. Some workers have tried to give it by the rectum, but it is doubtful if it can be absorbed in sufficient concentration to be effective.

The time of administration:- Experience has shown that this drug should not be administered on a full stomach. Christopherson⁷ found that it was best tolerated if injected about two hours before the mid day meal. Faust and Meleney⁸ recommend that the injections should be given mid-way between breakfast and lunch time. This solution should not be kept

Dosage:- Most observers are in agreement that the initial dose should be $\frac{1}{2}$ gr. of tartar emetic dissolved in about 5 cc. of normal saline. If this is not followed by any untoward symptoms the dose is increased slowly by about $\frac{1}{2}$ gr. each time (the injections being given at intervals of 1-2 days.) till a maximum of 2-2 $\frac{1}{2}$ gr. is reached. In the absence of toxic symptoms, this dose is kept up till the course is complete.

On no account should the total amount, given to any one patient be more than 25-30 gr. in one course. If at the end of one course, it is considered necessary to give more, a period of 1-2 months should be allowed to elapse before starting the second course.

Christopherson's method:- He started the treatment with an initial dose of $\frac{1}{2}$ gr. of tartar emetic, dissolved in 20 minims of distilled water; this was again diluted with 2 volumes of distilled water before injecting. The dose was increased by $\frac{1}{2}$ gr. every other day till a maximum of $2\frac{1}{2}$ gr. was reached. When giving the larger doses, the total amount was made up to 10 c.c. with normal saline. The full course consisted of 25-30 gr. administered in a period of 4-5 weeks.

For routine use, a stock solution was made up in a sterile vaccine bottle, with a rubber cap, in a strength of $\frac{1}{2}$ gr. to 1 c.c. of distilled water, and for use this was diluted with 5 c.c. of sterile normal saline. This solution should not be kept for more than 1-2 days.

Modifications of Christopherson's method:- Low and Newnham⁹ found that a total of 20-30 gr. of antimony was sufficient to effect a cure, but they preferred to give their injections twice a week instead of on alternate days. The dosage was the same as employed by Christopherson. They diluted the injections in large quantities (up to 60 c.c.) of normal saline.

that in the year 1919-20, the treatment was started on a large scale at the Kasr-el-Ainy hospital in Egypt by Day¹⁰; as many as 200 new cases being treated each month. It was considered useless to employ bulky injections, and a freshly prepared 6% solution of the drug (containing 1 gr. in 1 c.c.) in sterile water was found to be quite safe in expert hands, with the advantage that up to 2 gr. could be given with a small syringe and a small needle. Such a concentrated solution should be used by experts only, because any leakage of the drug outside the vein would be dangerous. After a study of over 1,000 cases, Day recommends an initial dose of 1 gr., a second of $1\frac{1}{2}$ gr., and subsequently 2 gr. doses on alternate days. The total he suggests should be $22\frac{1}{2}$ gr. given over a period of four weeks. Cawston¹¹ considers that potassium antimony tartrate is less toxic when dissolved in saline solution than in distilled water. He holds that if the dose never exceeds $1\frac{1}{2}$ gr., lack of toleration is rarely experienced. In schistosomiasis japonica, Tootel¹² used smaller doses than those recommended by Christopher-son, and Day. He began with a dose of $1/6$ gr. (.01 Gm.) using 0.5 c.c. of a 2% solution, and increased the dose by the same amount till he had reached $1\frac{1}{2}$ gr. (0.1 Gm.) using 5 c.c. of the same solution. In cases with nausea, headache, diarrhoea etc. he reduced the next dose by 1 c.c. He found

that most of his cases could be cured by 17 injections given in an average period of 38 days.

provided Faust and Meleney⁸ recommended a more intensive course, starting with a larger initial dose, and working up quickly to the limit of the patient's tolerance. They believe that if the patient can be kept saturated with the drug, by giving daily injections, a successful course of treatment can be completed in about 18 days.

They use fresh solutions of the drug in 10 c.c. of fresh distilled water (this being kept constant for all doses of the drug, because even the larger doses will not exceed a concentration of 2 %). The initial dose for an adult is 0.05 Gm. ($\frac{3}{4}$ gr.), increased each time by .025 Gm. until a slight reaction is produced (usually about .175-.2 Gm.). Injections are given daily for periods of three days followed by a day of rest, keeping the dosage just below the limit of tolerance, till 1.5-2 Gms. of the drug have been given.

only They consider this method ideal for early cases in good general condition, and have cited the case of an American Naval Officer who was cured with an intensive course, given in 17 days, and suffered from no ill effects beyond a little nausea. They advocate caution when using this drug in late cases, especially those with cirrhosis of the liver.¹³

nerosis In women and children, the dosage has to be proportionately reduced. $1\frac{1}{2}$ gr. of the tartar emetic is considered the maximal single dose, and a course

of 12-14 gr. is usually enough. In children it is a safe rule to give a grain for each year of age, provided the maximum does not exceed 0.003 Gm. per kilo of body weight.

In very young children, it may be impossible to employ this drug, because the veins are too small to allow for safe intravenous injection. In these cases, other preparations which can be given subcutaneously, or intramuscularly have to be tried.

It is difficult to follow hard and fast rules in connection with the dosage, when dealing with a potent drug like tartar emetic and every case has to be judged on its own merits. In any case, a start should be made according to the principles laid down, but the dosage for subsequent injections is best judged from the effect produced by the last injection, keeping a very careful look out for any toxic symptoms or complications.

Toxic effects of tartar emetic:- These may be (1) Local, or (2) General. The local effects are only due to faulty technique resulting in the leakage of the drug outside the vein. The patient complains of intense pain at the site of the injection; this may be treated by pulling back the piston of the syringe to aspirate as much of the leaked drug as possible, and then withdrawing the needle. Hot fomentations should be applied over the part. If necrosis follows, it may have to be aspirated or incised, with rigid asepsis to prevent infection.

faeces, sweat, and the sputum, most of it tends to

accumul(2) General:- These may again be immediate or delayed. The former come on during, or soon after the injection. They indicate either a hypersensitivity on the part of the patient to the drug, or that his limit of tolerance is being approached.

alcohol There may be a flushing of the face and neck, and a metallic taste in the mouth. Some complain of a feeling of constriction, or tightness around the chest, with violent fits of coughing. Giddiness, nausea, vomiting, and abdominal colic may indicate intolerance in some cases. McDonagh noticed a usual swelling of the lips, and the tongue in some of his cases. acute or chronic antimony poisoning. The

former Unless these symptoms are too severe, no active treatment beyond stopping the injection, and rest is necessary, and they usually pass off within a short time. In cases where they produce marked discomfort, the dosage may have to be reduced, or the next injection may be postponed. Rarely these symptoms may be so severe, that the drug may have to be discontinued, and replaced by some less toxic preparation. its suspension.

Christopherson¹⁴ has recently stated, that if a subcutaneous injection of $\frac{1}{4}$ gr. of omnopon is given ten minutes before the tartar emetic, most of these unpleasant symptoms can be avoided.

The delayed toxic symptoms due to this drug come on slowly, after a few injections have been given. Though the drug is partly excreted in the urine, and faeces, sweat, and the sputum, most of it tends to

accumulate in the body. If its concentration in the body goes beyond a certain limit, which differs in different individuals, toxic symptoms are produced. According to Cawston¹⁵ heavily infected cases, and vegetarians can stand larger doses, and alcoholics can tolerate very small doses only.

A certain amount of rheumatic pains in the joints, and muscles are often complained of when four to five injections have been given; these, unless very severe, should not be taken very seriously and usually pass off in a few days. The actual toxic symptoms may resolve themselves into those due to acute or chronic antimony poisoning. The former are characterised by nausea, vomiting, giddiness, diarrhoea, hyperpyrexia, delirium, and cramps in the calf muscles. In cases where the poisoning is of the chronic type there may be general weakness, loss of weight, anaemia, epigastric pain, jaundice, increasing albuminuria, cracked and ulcerated tongue, and diarrhoea. Persistence of any of these symptoms indicates that the drug is not being tolerated, and calls for its suspension. In view of the cumulative action of the drug, extreme caution is necessary, when nearing the limit of tolerance in any given case, and the drug must be discontinued when 25-30 gr. have been given. Archibald and Innes¹⁶ have reported a case of death after 33 gr. of tartar emetic had been administered. A post mortem examination was performed, and no living schistosome worms were found in the body.

tal accommodation for every case requiring treatment.

As this patient had been suffering from influenza, a few days before his death, it is not certain if death was due to antimony poisoning. Christopherson¹⁷ subsequently commented on this case, and was of opinion that death was most probably due to influenza, or some other cause.

Another case has been recorded by Breinl and Priestley,¹⁸ where a young man who was under treatment for infective granuloma of the groin, with tartar emetic, died suddenly after the administration of 1.74 Gms. of the drug. He appeared to be quite well until a day before his death, when he suddenly became very ill with severe vomiting, and collapsed. On autopsy, the heart and the liver showed fatty degeneration.

In Khalil's experience,¹⁹ out of 284,934 cases treated with tartar emetic there were only six deaths.

Most observers, who have had experience with this drug, have advocated the use of caution and circumspection, and emphasise the danger of being too heroic or careless.

Tootel¹³ treated all his cases in hospital, and recommends hospitalization for all cases under treatment with tartar emetic. This, in his opinion, ensures better supervision, and increases the chances of completing the full course of treatment in most cases. The obvious drawback of this method is, the expenditure involved, and in some of the endemic areas, where large numbers of people are infected, it would be practically impossible to provide hospital accommodation for every case requiring treatment.

Khalil and Day²⁰ on the other hand, have used this drug extensively in the treatment of the out-patients, without any ill effects. The routine followed in the various annexes, opened for the treatment of schistosomiasis in Egypt, is that the patient is given accommodation to lie down for an hour or two after the injection, and then allowed to proceed home.

Contraindications:- This drug is obviously contraindicated in young children, and very fat people, where the veins are hard to find. Tartar emetic should never be given to people suffering from advanced liver, heart, or kidney disease. It is also contraindicated in the aged.

Before commencing a course of antimony therapy, any other parasitic disease e.g., malaria, dysentery (amoebic), or hook-worm infection should be eradicated, (Day)²¹.

Severe and persistent toxic symptoms, and increasing albuminuria have already been discussed as signs of intolerance, and a signal for discontinuing or postponing further treatment.

Christopherson and Gloyne²² have reported that some people may develop a hypersensitiveness to the drug after they have had a few injections; this according to them is due to a bio-chemical action of tartar emetic, not unlike the anaphylaxis seen after the administration of a foreign protein to an animal.

The action of antimony:- Christopherson is of

opinion that the drug first acts on the adult worms in the portal blood stream, and later on kills the miracidia inside the ova.

Faust and Meleney⁸ tried the effect of varying dilutions (1 in 600 to 1 in 42,000) of sodium antimony tartrate (vide infra) on the adult S. japonicum worms obtained from a dog, in vitro and concluded that:-

1. Death of the worms seemed to take place from the posterior extremity forwards, as evidenced by a granular change of the body protoplasm, developing into opacity. The ventral and the oral suckers were the last organs to lose motility.

2. All worms were killed, even by the 1 in 42,000 dilution of the drug, in one hour. The higher concentrations were lethal in correspondingly less time; 1 in 1,200 solution killed the worms in one minute.

3. The females were found to be slightly more resistant than the males.

It would seem from the above, that if a concentration of the drug, of about 1 in 42,000 or above could be produced in the host's blood, even for a short time, all worms should be killed. It is however doubtful as to what proportion is absorbed by the tissues after the injection.

If the total blood volume was estimated as 8.8 % of the body weight, or 88 c.c. of blood per kilo, and if the average maximum dose of the drug was considered to be .003 Gm. per kilo, then the

calculated concentration of the drug at the time of the injection would be about 1 in 29,000. Such a dosage, if frequently repeated should, in their opinion, soon kill all the worms in the host's body. of the Christopherson and Newlove²³ tried the effect of tartar emetic 1 in 46 on freshly passed ova of S. haematobium, and found that they failed to hatch. He is of opinion, that in vivo the drug permeates through the shells, and kills the miracidia. This action of the drug is of considerable value in the prophylaxis of the disease,²⁴ because the ova fail to hatch after the patient has been under treatment for some time. According to Khalil²⁵, the prevention of hatching by the action of 1 in 46 tartar emetic in vitro is due to its effect on the osmotic pressure of the solution, and miracidia are not affected by dilutions of the drug that can be possibly attained in vivo. During treatment, but it is some times very difficult. Christopherson states that tartar emetic is lethal to all stages in the life history of the parasites, and the susceptibility varies in the following order. The adult worms are most sensitive, then the miracidia, and the eggs are the last to die. Dye²⁶ also endorses Khalil's view with regard to the prevention of hatching of the ova in vitro by tartar emetic as being due to its effect on the osmotic pressure. According to him also the parent worms are least resistant to the action of tartar emetic, than the cercariae, the miracidia, and the ova are most resistant. eosinophilia could be due to

causes also, and hence the blood counts may often be misleading. Faust and Meleney have challenged Christopherson's view, that the ova are killed in the tissues

Fairley found that the complement fixation of the adult host by antimony. They believe that test formed a valuable aid for checking the effect the concentration of the drug is higher in the lumen of treatment. In several cases, the test became of the gut, due to its excretion, and the ova die progressively weaker as the patient improved. Here after their extrusion through the mucosa. They again, it is found that, though a strong positive support this view with the finding that if treatment may be brought down to a weak positive, by a course is temporarily suspended, shortly after the first of specific therapy, the test does not always failure of the eggs to hatch, viable eggs can again become negative, even in the successfully cured be obtained in three days. But as it has been found cases. In his experience with goats, experimentally that in most cases, dead eggs appear in the faeces, infected with *S. spindalis*, Fairley was unable to for a long time after the successful conclusion of a produce serologically negative results in spite of course of treatment, they must have been killed in the most extensive treatment. Though the complement the deeper tissues, and their further progress has fixation test is a valuable guide regarding the been entirely as inert foreign bodies.

effect of specific therapy, it falls short of being Test of cure:- Symptomatic improvement is a reliable test of cure.

usually noticed in almost all cases within a few days

Christopherson considers the condition of of commencing treatment, but it is some times very the ova, as seen in the urine or the faeces, as an difficult to be certain that all worms and ova have important point for gauging the effect of treatment. been successfully destroyed.

In his opinion if all the ova fail to hatch on

Differential leucocytic counts usually give repeated examination during, and after the course a rough idea of the effect of treatment in most cases. of treatment, the case has probably been cured. The As the worms start dying out there is a diminution earliest change seen in the ova is that they become in the percentage of eosinophil leucocytes; but this blackish in colour, and their contents appear to be can hardly be used as a test of cure, because even in granular. The double contour is lost. The most cases which have been cured, the count does not reliable test of their death, is their failure to always approach normal. Archibald and Innes regarded hatch on the dejecta being diluted with water. the eosinophil count, as a reliable index of improve- Christopherson recommends that, if all ova are not ment in cases under treatment, but Christopherson¹⁷ dead after the administration of 30 gr. of tartar has stated that eosinophilia could be due to other

causes also, and hence the blood counts may often be misleading.

Fairley²⁷ found that the complement fixation test formed a valuable aid for checking the effect of treatment. In several cases, the test became progressively weaker as the patient improved. Here again, it is found that, though a strong positive may be brought down to a weak positive, by a course of specific therapy, the test does not always become negative, even in the successfully cured cases. In his experience with goats, experimentally infected with S. spindalis, Fairley²⁸ was unable to produce serologically negative results inspite of the most extensive treatment. Though the complement fixation test is a valuable guide regarding the effect of specific therapy, it falls short of being a reliable test of cure.

Christopherson considers the condition of the ova, as seen in the urine or the faeces, as an important point for gauging the effect of treatment. In his opinion if all the ova fail to hatch on repeated examination during, and after the course of treatment, the case has probably been cured. The earliest change seen in the ova is that they become blackish in colour, and their contents appear to be granular. The double contour is lost. The most reliable test of their death, is their failure to hatch on the dejecta being diluted with water. Christopherson recommends that, if all ova are not dead after the administration of 30 gr. of tartar

emetic, the patient should be given another course after waiting for one to two months.

Franca^{29,30} studied the action and the effects of tartar emetic, and came to the conclusion that, though the eggs may have a normal outline, the embryo is usually structureless and granular. He also found that most of the eggs were smaller in size, which he believed to be due to their being prematurely deposited, or aborted, due to the action of the drug on the female worms. He therefore suggests that the results of treatment may be checked by the measurement of the ova passed out (ovometry). This method would be far too laborious for routine use, and the variations in the size of the ova may complicate its interpretation.

The most reliable test of cure would be the absence of live ova in the dejecta, on repeated examination, for some time after the conclusion of a course of treatment with a specific drug.

Results of treatment with tartar emetic:- Symptomatic relief is usually felt within a few days of the commencement of treatment. The more urgent symptoms, e.g., dysuria, griping, and epigastric pain etc. are first relieved, and if the treatment is continued, there is a marked improvement in general appearance, with gain of weight and feeling of well-being.

The blood in the urine and the faeces soon disappears, and as already stated, most of the ova that come away show degenerative changes.

Libby³¹ tried tartar emetic in cases of schistosomiasis japonicum, and found that 4-10 gr. of the drugs were sufficient to make the ova disappear from the stools. He is of opinion that in suitable cases, if the drug is going to be effective at all, marked improvement should be noticed after about 12 gr. have been given. but on account of the dangers associated Phease³² is of opinion that treatment is usually incomplete in about 20 % of the cases, and recommends that the cases should be kept under observation for two years, with periodic examination of the dejecta for ova, before pronouncing them as cured. Most of Christopherson's cases were found to be negative on examination for ova, one to two years after treatment.

Khalil³³ found that in a series of 1,000 cases, treated with tartar emetic, only 43.2 % could be said to be definitely cured. Tootel reported cure in 50 % of his cases. Good results have been obtained by several other observers e.g., Wiley³⁴, Taylor^{35,36}, Newnham³⁷, Sanders and Priston³⁸, Coleman³⁹, Smith⁴⁰, and Spence⁴¹ have found this drug to be very useful in all forms of schistosomiasis, provided the treatment is started in the early stages of the disease. Wilson⁴² reported useful results after rectal administration of tartar emetic, in 1922. Barcroft and Anderson (1925)⁴³ advocated the use of tartar emetic per rectum, in cases where intravenous toxic to injections could not be given. Christopherson⁴⁴ said that it was very doubtful if this could be of any use. Dye⁴⁵ also expressed his doubt with regard to the

absorption of the drug from the large intestine. Lathram⁴⁶ found it useless in a typical case for treatment. It may be concluded from the above that tartar emetic is of definite value in the treatment of all forms of schistosomiasis both as a curative and as a prophylactic, but on account of the dangers associated with its use, it should be administered with great care.

Other preparations of antimony:— Colloidal antimony (Antimony sulphide) was first tried by McDonagh,⁴ and he found that it was less potent than tartar emetic in its action on the schistosome worms. In very young children, and other cases where treatment by injections is not practicable, Wylie⁴⁷ has recommended the use of an ointment of metallic antimony. Good results have been obtained by its use in kala-azar. The drawback of this method is that the results are very slow.

Sodium antimony tartrate $2(\text{NaSbO} \cdot \text{C}_4\text{H}_4\text{O}_6) \cdot \text{H}_2\text{O}$. :— This drug is as effective as tartar emetic, and is said to be less toxic; it is difficult to obtain in a pure state. If this drug is used the solution must be freshly prepared immediately before injection.

Brahamchari⁴⁸ found that sodium antimony tartrate, and potassium antimony tartrate were equally toxic to guinea pigs. Cawston⁴⁹ was of opinion that the sodium salt was less toxic if a fresh solution was used, and the dosage was properly regulated. Tai⁵⁰ found sodium

antimony tartrate more useful than colloidal antimony.

Miyagawa⁵¹ has said that slightly alkaline solution of sodium antimony tartrate (Neostibnal), is as effective as tartar emetic and less toxic. Though this drug is reputed to be less toxic than tartar emetic, its comparative instability makes it unsuitable for routine use.

Brahamchari tried to find a less toxic preparation of antimony for use in the treatment of kala-azar, and prepared the antimony tartrates of urea, ammonia, and aniline. On comparing their effects on guinea pigs, he found that out of these three the ammonium salt was the least toxic. As none of these drugs offered any marked advantage over tartar emetic, they have not been tried to any extent in the treatment of schistosomiasis.

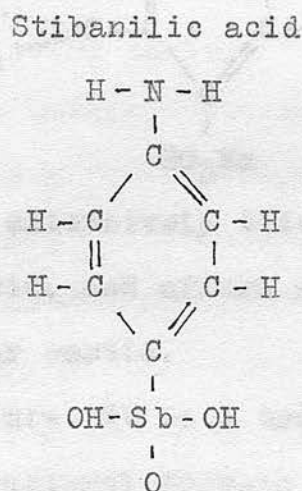
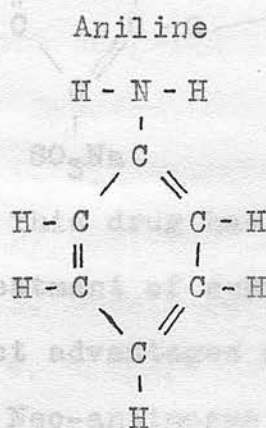
Shattuck and Willis⁵² in 1928, tried antimony sodium thioglycollate, and antimony sodium thioglycollamide in their cases of schistosomiasis, and have reported good results. The drug was found to be less toxic than tartar emetic, but it was unstable in solution. Messrs Hynson, Westcott, and Dunning of Baltimore, have marketed a solution of antimony sodium thioglycollamide in ampoules (.4 % strength), which is claimed to be indefinitely stable.

Shattuck⁵³ tried sodium antimony thioglycollamide in 14 cases in 1931, and found it to be less toxic, and more effective than tartar emetic. It was indefinitely stable, but too expensive for general use.

It was found that the organic compounds of antimony, where the antimony was attached directly to the C, and not through oxygen as in the emetic type of compounds, did not give rise to bronchial irritation and pneumonia in experimental animals. These preparations were found to be less toxic, could be given at shorter intervals, and a course of treatment could be completed in a lesser amount of time.

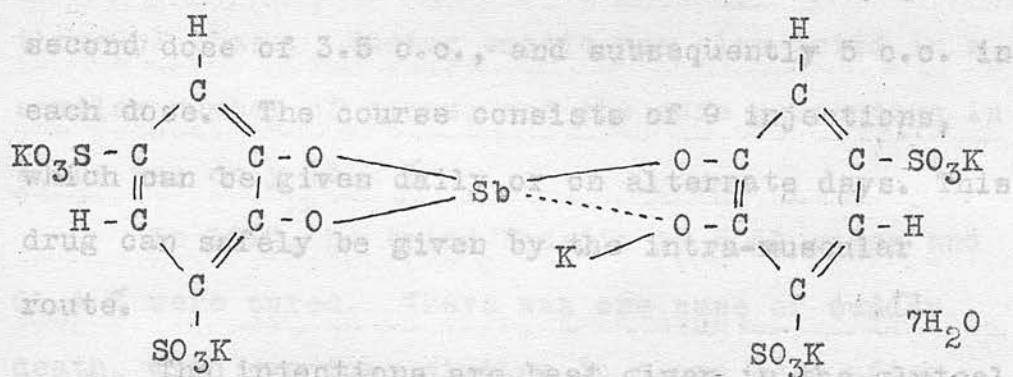
⁴⁸ Brahamchari prepared urea stibamine, and found that it was 23 times less toxic as compared with tartar emetic in guinea pigs.

The basis of all these compounds is stibanilic acid, formed by substituting the antimononic acid residue $\text{SbO}(\text{OH})_2$ for a hydrogen atom in aniline.

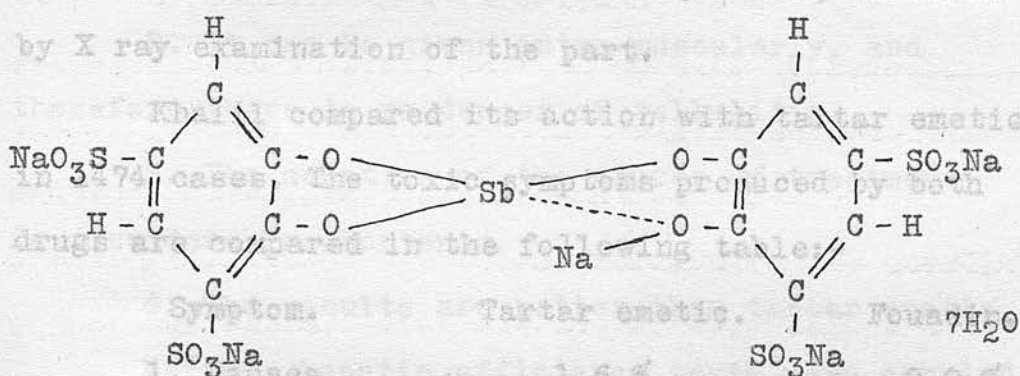


The earlier antimony catechol compounds were found to be very sparingly soluble, therefore an attempt was made to add the sulphonilic group HSO_3 with a view to increase their solubility, and antimosan was prepared, which was found to be more soluble, more stable, and neutral in reaction.

Antimosan.



Necantimosan (Fouadin).



Neo-antimosan or Fouadin:- It is a trivalent antimony compound, and its structural formula (vide supra) is expressed as antimony-III-pyrocatechin-disulphonate of sodium (Smichdt).⁵⁴

It is a white powder containing 13.5 % of antimony. It is available in solution containing 0.0085 Gms. of trivalent antimony in one c.c.

^{55,56} Khalil tried this drug in a large number of cases, during 1929-30, with very satisfactory results.

He started with an initial dose of 1.5 c.c., gave a second dose of 3.5 c.c., and subsequently 5 c.c. in each dose. The course consists of 9 injections, in which can be given daily or on alternate days. This drug can safely be given by the intra-muscular and route. were cured. There was one case of sudden death. The injections are best given in the gluteal region, and if given deep down they are usually accompanied by very slight pain. The pain after the injections according to Khalil, is so slight that it can be easily borne by children. The drug is absorbed within 6 minutes after injection, as found by X ray examination of the part. muscally, and therefore Khalil compared its action with tartar emetic in 1474 cases. The toxic symptoms produced by both drugs are compared in the following table:-

Symptom.	Tartar emetic.	Fouadin.
1. Nausea.	1.6 %	0.0 %
2. Vomiting.	3.8 %	0.36 %
3. Dizziness.	0.64 %	0.018 %
4. Cough.	9.64 %	0.0 %
5. Abscess.	5.3 %	0.13 %
6. Local induration.	2.4 %	0.0 %

He has also remarked that this drug is safer for the treatment of schistosomiasis in cases suffering from pulmonary tuberculosis, because it does not give rise to attacks of coughing which may precipitate haemoptysis. but it should not be given intra-v

Out of 1,000 cases treated with Fouadin, 68.6 % were cured, and on careful examination of the

dejecta three months later, ova were found in only three of these. Tartar emetic was also tried in a similar number of cases, and the cure percentage in these was only 43.2 %

In 1929,⁵⁵ he tried Fouadin in 2041 cases and 61.4 % were cured. There was one case of sudden death, with symptoms similar to those seen after tartar emetic, one day after completing the course of treatment.

According to Khalil, Fouadin has the following advantages over tartar emetic:-

1. It is less toxic.
2. It can be given intra-muscularly, and therefore there is no danger of cellulitis.
3. The duration of the course of treatment is considerably shortened.
4. The results are better than tartar emetic.

Various hepatic efficiency tests were carried out in the Research institute and the Endemic diseases hospital, Cairo, in 1932, before and after the administration of Fouadin. In spite of the fact that some of the patients were already suffering from enlargement of the liver, hepatitis, cirrhosis of the liver, and jaundice, no apparent damage could be demonstrated after a normal course of Fouadin.

⁵⁷ Orenstein has recently opined that Fouadin is equally efficacious, and less toxic as compared with Sodium antimony tartrate, but it should not be given intra-venously, and not more than three injections in a week.

According to Peter⁵⁸ 50 % of antimony is excreted in the urine after injection of Fouadin, and 4 % in the faeces, the rest being stored in the alimentary canal, liver, spleen, kidneys, and the heart.

Low and Franklin⁵⁹ gave a course of 10 injections of Fouadin in 13 days, to a case of schistosomiasis japonicum in an English man 6 months after infection. The ova rapidly disappeared from the stools (none being seen after 9 days), and there were no toxic symptoms. The total quantity of the drug administered was 45 c.c.

Browne⁶⁰ also has reported apparent cure of schistosomiasis japonicum with 45 c.c. of Fouadin.

Lee and Chung⁶¹ tried the drug in several cases, and though temporary improvement was noticed in practically all of them, some relapsed. The question of possible reinfection did not arise, because most of them were residing in a nonendemic area.

Lee⁶² tried the drug in experimentally infected rabbits, by the intravenous as well as intramuscular routes. He found that the ova disappeared from the stools in all the cases after varying intervals of time, but the cure appeared to be incomplete in some of them as seen by the reappearance of the ova some time later. He got better results with the intramuscular injections as compared with the intravenous. He emphasised the fact that the disappearance of the ova from the stools, during treatment, should not be taken as a criterion of cure.

He concludes "Fouadin, does, therefore possess therapeutic value in the treatment of schistosomiasis japonica in rabbits, though in many respects it falls short of an ideal specific."

Kan and Yao⁶³ tried Fouadin in 117 cases of schistosomiasis japonicum, and found it very useful.

65 % of the cases were cured, and there were no toxic symptoms beyond nausea in 3 cases.

Khaw⁶⁴ tried a new sample of the drug, containing 11 % antimony (1 c.c. contained 14.3 m. gm. of antimony), in rabbits experimentally infected with

S. japonicum. Out of 20 rabbits, 14 were cured, and

5 died of schistosomiasis aggravated by the treatment.

One of the rabbits remained uncured. The

average amount of the drug used was 6.42 c.c. given

over a period of four weeks.

Judging from these results, Fouadin would

appear to be definitely superior to tartar emetic,

it being less toxic and more effective. It has the

additional advantage that it can be injected intra-

muscularly.

Emetine hydrochloride:-

The use of emetine in schistosomiasis, was

apparently first noted by Hutcheson⁶⁵, in cases of the

Far Eastern type of the disease in 1913.

Boulliez⁶⁶ tried it in 1915, but his results

were indefinite. Later Diamantes⁶⁷, Erian⁶⁸, and others

found that it had a definite anthelmintic action

against the schistosome worms.

At the end of treatment the

Chemically, the drug is a hydrochloride of emetine (Methyl cephaeline, $C_{15}H_{21}NO_2$), an alkaloid obtained from Ipecacuanha, which is an amorphous white powder (turns yellow on keeping), soluble in alcohol, ether, or chloroform, but not in caustic alkali.

Emetine hydrochloride can either be obtained from Ipecac, or can be prepared synthetically, with not more than 9 % of water. It occurs as a white or a very slightly yellowish crystalline powder, freely soluble in water or alcohol.

Route of administration:- If given orally, it acts as a powerful emetic, but it can safely be injected by the intravenous, subcutaneous, or intramuscular routes.

Diamantes claimed that in the treatment of simple, non-septic haematuria, caused by *S. haematobium*, emetine intravenously in doses of 0.05 to 0.1 Gms. was very useful.

Day (1921)⁷¹ found that emetine was effective against schistosomiasis if given in large doses, upto $3\frac{1}{2}$ gr. for each injection, and he preferred the intravenous route. Later on he had good results in some cases with the same doses as used in the administration of tartar emetic; starting with $\frac{1}{2}$ gr., working upto about 2 gr., and giving a total of $22\frac{1}{2}$ gr. in 12 doses, during a period of four weeks.

Bonnet⁶⁹ started with $\frac{1}{3}$ gr. and slowly increased it to $1\frac{1}{2}$ gr., given on alternate days, till a total of 18 gr. was reached. At the end of treatment the

haematuria disappeared, and the eggs showed degenerative changes. He considered emetine given intravenously, to be the best treatment for schistosomiasis.

is that Christopherson gave 15-20 gr. in $1\frac{1}{2}$ gr. doses, during a period of 6-8 weeks, and considered it second in value to tartar emetic.

hydroc⁷⁰ Cawston has claimed cures in all cases of patients under 15 years of age, who were able to tolerate 12-15 gr. of the drug in not more than 24 days, and he has remarked that not only the dosage, but the length of treatment also is important when this drug is used.

whom th⁷¹ Day found that after completing a course of emetine, live ova could still be seen in the dejecta, but they were not found on further examination 5 months later. This he believes is due to the drug having a cumulative action.

Lee⁷² has pointed out that in the treatment of schistosomiasis japonicum, emetine is slower, and less satisfactory than tartar emetic. Kan and Yao also found Emetine unsatisfactory in the Far Eastern type of the disease.

suitable On the other hand Fairley⁷³ found that in animals, experimentally infected with S. spindalis, emetine gave better results than tartar emetic.

daily. Emetine is a powerful cardiac depressant, and deaths have been reported from heart failure due to its use. Numbness, and heaviness of the limbs are often complained of, and in some cases it may go on to peripheral neuritis. Its use is usually accompanied

by nausea, and in larger doses it may act as a powerful emetic.

Another disadvantage in the use of this drug is that it is too expensive for extensive use as a prophylactic.

If at any time during a course of emetine hydrochloride, tachycardia, weakness of the limbs, or other signs of cardiac depression become manifest, the drug should be discontinued.

Emetine is best suited in the treatment of schistosomiasis in:--

(a) Very young children, and fat people in whom the veins are inconspicuous. This indication has become less important since the advent of Fouadin.

(b) Cases where tartar emetic has produced an abscess.

(c) People who are intolerant to antimony.

(d) Cases with advanced hepatic or renal disease.

(e) Cases in which schistosomiasis is complicated by amoebiasis.

⁷⁴Gordon tried to find a preparation of emetine suitable for oral administration. He treated two batches, each of 14 children, in West Africa, with hypodermic injections of emetine hydrochloride $\frac{1}{2}$ gr. daily, and emetine periodide by the mouth 1 gr. three times daily in milk respectively. After 8 days, all cases in the former group, and 12 out of 14 in the latter, had stopped passing ova. In a later communication ⁷⁵he states that on subsequent examination, 5 out

of 8 out of those treated with emetine hydrochloride, and 4 out of 7 in the latter group had again started, passing ova.

Recently Tsykalas⁷⁶ has published his notes of 3,800 cases of schistosomiasis treated with emetine, giving a total of 1.12 Gms. of the drug intravenously, in 10 injections. He claims a cure percentage of 90.5. He has formulated the following ten rules for the use of emetine in the treatment of schistosomiasis:-

1. Total dosage should be 1.25 Gms.
2. Treatment should be completed in 10-14 days.
3. Begin with a big dose.
4. Injections should be given daily.
5. Regulate dosage by body weight, and not by age.
6. May be given intra-venously, or intra-muscularly.
7. Start treatment as soon as possible after diagnosis.
8. Watch the heart carefully during treatment.
9. Give rest for at least two months before repeating course.
10. The drug must be pure.

The value of emetine in the treatment of schistosomiasis, has gone down with the discovery of Fouadin, which can also be given intra-muscularly, and is less toxic and more effective. It may still prove useful in some cases, who are intolerant to antimony, or in those suffering from amoebic dysentery as well.

If a preparation of emetine (like emetine periodide) suitable for oral administration is perfected, as a cure for schistosomiasis, by more extensive trial it may be very useful. The absence of complications,

and a haemoglobin percentage of 70, or above. Later

Other drugs:-

A large number of drugs have been tried by the various workers, and though good results have been claimed for some of them, they have not been found to be suitable for the treatment of the disease on most of the cases, it was too toxic for general use, a large scale.

In 1928, Gawton recommended the use of carbon tetrachloride, given in doses of 3 c.c. each morning for three consecutive days. He claimed to have succeeded in producing degenerative changes in the ova, by the use of this drug. The editor of the Chinese Medical Journal, has appended a note to one cases of schistosomiasis japonicum without effect. Job has recorded failures with the use of neo-salvarsan.

Reference has already been made to the use of quinine. It was tried by observers in the Far East,

and though symptomatic improvement was often produced, it was not effective in getting rid of the parasites. Recently Fisher, on finding that acriflavine was lethal to schistosome cercariae, in the presence of human blood serum, tried the drug in cases of

Petzatakis gave daily intra-venous injections of calcium chloride, in a 10 % solution, giving 0.5-1 Gm. in 10 days, and then every second day for in a 2 % solution, on an empty stomach, regulating the dosage according to the body weight. For people favourably with emetine and tartar emetic in early weighing 80 kilo Gms. or less, he gave .02 Gms. per cases.

kilo, and the dosage was correspondingly reduced for

⁷⁹ Tootel tried mercurochrome 220 soluble, in some of his cases of schistosomiasis japonicum, in 1926, with good results. He recommended its use in all early cases, in the absence of complications, and a haemoglobin percentage of 70, or above. Later ⁸⁰ on he found that mercurochrome was some times liable to give rise to severe reactions, with chill and hyperpyrexia. He came to the conclusion, that though the drug did produce definite improvement in most of the cases, it was too toxic for general use.

^{81,82} In 1928, Cawston recommended the use of carbon tetrachloride, given in doses of 3 c.c. each morning for three consecutive days. He claimed to have succeeded in producing degenerative changes in the ova, by the use of this drug. The editor of the Chinese Medical Journal, has appended a note to one of his communications on the subject in that journal, advocating caution in the use of this drug, which if given in the large doses recommended, is apt to be dangerous.

⁸³ Recently Fisher, on finding that acriflavine was lethal to schistosome cercariae, in the presence of human blood serum, tried the drug in cases of schistosomiasis in Yakusu, in the Belgian Congo, both by the mouth, and by injections. He gave the drug in a 2 % solution, on an empty stomach, regulating the dosage according to the body weight. For people weighing 20 kilo Gms. or less, he gave .02 Gms. per kilo, and the dosage was correspondingly reduced for In some carefully selected cases, it may still prove to be the ideal drug.

heavier people, those weighing 60 kilo Gms. or more getting .012 Gms. per kilo. The total quantity of the drug administered, did not exceed 0.7 Gms. in any case. Given in these doses, it did not produce any toxic symptoms. His cases became symptom free in 3 days, and the ova were found to be degenerate in a week.

84 Fakhry tried acriflavine in cases of ankylostomiasis, and schistosomiasis. He found it useful in the former, but ineffective in the latter. Khalil⁸⁵

Symptomatic treatment:-
found that though acriflavine gave symptomatic

A lot can usually be done towards relieving relief, it did not destroy the parasites.

the sufferers from schistosomiasis by adequate symptomatic treatment.

Several other drugs, e.g., iron, male fern, methylene blue, thymol, benzene etc. have been tried by Briscoe⁸⁶ and others, without effect.

From the results obtained by most of the inflammatory process in the bladder of the workers, in connection with the treatment of schistosomiasis with the various drugs, it may be concluded, These may be treated with lavage of the affected part with a mild antiseptic e.g., boric lotion. Urinary that tartar emetic, and Fouadin have the best claims antiseptics e.g., cubebs, copaiba, or saucal wood oil out of the various preparations that have been tried.

can be used in cases with cystitis, and in the intestinal type of the disease salol, or thymol given Khalil, and others, Fouadin appears to be more useful, internally, may be useful.

In advanced cases, specific therapy may be of and economy is an important consideration, tartar little or no avail. The permanent tissue changes emetic may still be employed to advantage in expert produced by the parasites are only amenable to hands.

surgery.

The position of emetine in the treatment of this disease, is comparatively secondary, and the Lasbrey and Coleman have recommended the use of tartar emetic, prior to operation in cases with indications for its use (vide supra) are limited. surgical complications. This, in their opinion, In some carefully selected cases, it may still prove to be the ideal drug.

During the last year, acriflavine has been favourably reported upon by Fisher, and if his claims are confirmed by other observers, this drug may possibly take a more important position in the future treatment of schistosomiasis.

From the observations made by various workers it has been found that the various drugs are about equally effective against all the three forms of human schistosomiasis.

Symptomatic treatment:-

A lot can usually be done towards relieving the sufferers from schistosomiasis by adequate symptomatic treatment.

In the earlier stages of the disease, when the ova start appearing in the dejecta, there may be an inflammatory process in the bladder or the rectum. These may be treated with lavage of the affected part with a mild antiseptic e.g., boric lotion. Urinary antiseptics e.g., cubebs, copaiba, or sandal wood oil can be used in cases with cystitis, and in the intestinal type of the disease salol, or thymol given internally, may be useful.

In advanced cases, specific therapy may be of little or no avail. The permanent tissue changes produced by the parasites are only amenable to surgery.

⁸⁷
Lasbrey and Coleman have recommended the use of tartar emetic, prior to operation in cases with surgical complications. This, in their opinion,

makes the subsequent progress of the case very rapid.

The various complications that may arise, have to be treated on general surgical principles.

Vesicular calculi, and new growths are best removed by operation. In advanced cases with rectal disease, Dolby and Fahmy⁸⁸ have shown that, although tartar emetic will destroy the ova, the papillomata, and the distressing symptoms accompanying them, usually persist. They had very good results in 8 cases by resecting the whole tube of the rectal mucous membrane.

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tional increase in the infection among the snails, leading to a greater number of cercariae being available to infect the adult host. This vicious circle can only be broken by active prophylaxis.

Occasionally, the disease has been known to take an epidemic form, resulting in considerable mortality. Khalil has described, what appeared to be an epidemic of schistosomiasis mansoni in the

Prophylaxis:-

Introduction:- In this section it is proposed to discuss the various problems in connection with the prophylaxis of schistosomiasis, with reference to the various endemic areas. The measures that would be most suitable in controlling a possible outbreak of the disease in India will be discussed in detail.

Though schistosomiasis is not as rapidly fatal as some other diseases e.g., plague, cholera, or yellow fever, it can produce a tremendous amount of suffering and debility, in areas where it is allowed to take a hold. In countries like Egypt, and China, large proportions of the population have been reduced to a state of chronic ill health, and the economic development and progress of the countries has been considerably hampered by this disease.

In countries, where the local customs and the habits of the people favour the spread of schistosomiasis, a vicious circle is soon established. As more human beings become infected, there is a proportional increase in the infection among the snails, leading to a greater number of cercariae being available to infect the adult host. This vicious circle can only be broken by active prophylaxis.

Occasionally, the disease has been known to take an epidemic form, resulting in considerable mortality. Khalil¹ has described, what appeared to be an epidemic of schistosomiasis mansoni in the

village Saft el Enab in Egypt, accompanied by heavy loss of life. In this village 83 % of the population were found to be infected with schistosomiasis.

Fortunately, as a result of the industrious efforts of the various workers, most points in connection with the disease are established beyond doubt, and consequently at first sight the control of infection would appear to be a comparatively simple matter. If the parasite could be effectively, and completely destroyed at any stage during its life cycle, the disease would become extinct.

It has been found on experience that complete destruction of the parasite at any stage is almost impossible, therefore the problem has to be attacked from every possible angle.

The problem is closely linked up with economic, political, religious, and racial questions, and the task is made more difficult due to the lack of co-operation, some times amounting to obstruction, on the part of the inhabitants of the endemic areas. As most of these people are uneducated, ignorant, and suspicious, considerable amount of tact is necessary in instituting changes in their traditional mode of life. Prophylaxis, in its application may be divided into:-

- (a) General prophylaxis, as applied to the community.

- (b) Personal prophylaxis, as applied to the individual.

S. mans (a) General prophylaxis:- It has already been discussed, that the schistosome worms have two phases in their life history; an asexual one in the intermediate (snail) host, and a sexual one in the mammalian host. The mode of passage from one host to the other has also been discussed. So the various methods by which the disease may be controlled are:-

1. The destruction of the adult worms and their ova in the adult host.
2. The prevention of the miracidia from gaining access to the intermediate host.
3. Destruction of the intermediate host.
4. Attack on the cercariae as they emerge from the intermediate host, and prevention of infection of the adult host.

Endeavour has to be made to apply all the four methods together where ever possible, because no single method can be relied upon to completely interrupt the life cycle of the worms.

(1) The attack on the parasite in the adult host:- This is carried out by administering adequate drugs which are known to destroy the adult worms and their ova.

This method can only be of use where man is the only definitive host. If natural infection exists in other animals also, even the most thorough treatment of all human cases would fail to produce the desired result.

It was hitherto believed, that in the case of treatment is continued. The effects of the various

S. mansoni, and S. haematobium, man was the only definitive host, but recently Cameron² has shown that monkeys found in St. Kitts in the Lesser Antilles are also naturally infected with S. mansoni. Infection with S. japonicum is quite common amongst cattle, goats, pigs, cats, dogs, rats, weasels etc., and consequently the treatment of human cases would be of little value in controlling the disease in an endemic area. The methods suitable in a country like China will be discussed separately.

Amongst other limitations of this method, may be considered the necessity of a prolonged course of treatment, with the possible danger of toxic effects on the host, and the fact that quite a number of lightly infected cases may escape diagnosis.

The method is most suitable in the case of schistosomiasis haematobium, because man is so far known to be the only adult host and it is comparatively easy to find the ova in the urine of most of the infected cases. Christopherson³ has stated, that if children were treated in schools, and taught sanitation, snails will not have to be killed in the water ways. But it has to be remembered, that it is not every child in these areas who goes to school. In countries like Egypt and Sudan, this method

As soon as a case is diagnosed, he should be given an adequate course of a reliable preparation of antimony. This first kills the ova in the body of the host, and the adult worms die later on if the treatment is continued. The effects of the various

drugs on the worms and their ova have already been discussed in detail. It may however, be repeated, that in most cases a course of about 30 gr. of a reliable preparation of antimony is considered sufficient to kill all worms.

Even in cases where the patients fail to turn up for further treatment, after the relief of the more urgent symptoms, they have become less dangerous to the community, and they usually return for further injections when the symptoms reappear. It is of the utmost importance to persuade all known cases, to complete the full course of treatment.

Active propaganda by means of lectures in the local languages, simple diagrams, or cinema films may induce some of the sufferers to come and apply for treatment.

The great advantage of this method is that there is an obvious relief of symptoms within a short time after the treatment is commenced; this ensures the patient's cooperation and encourages him to continue treatment. During the course of the treatment, the medical attendants should try to propagate the simple hygienic truths associated with the spread of this disease.

In countries like Egypt and Sudan, this method of prophylaxis has proved very useful; but as has already been stated, the problem is much more complex in China and Japan, on account of the existence of the various 'reservoir' hosts. The methods best suited to these countries will be discussed later.

1050 (2) The prevention of the miracidia from gaining access to the intermediate hosts:- Experience has shown that, this is usually the most difficult problem to tackle in an endemic area. The very fact that the disease has taken a hold in a given area, means that the sanitary control of the dejecta of the infected people must be unsatisfactory.

known It has been already noted, that the ova fail to hatch if the urine or faeces are not diluted with fresh water, and the miracidium dies within 24-36 hours (36-72 hours in the case of S. japonicum), if it does not meet its appropriate intermediate host.

storage Miyagawa (1916)⁴, studied the effects of various physical, and chemical conditions on the ova of S. japonicum, and came to the following conclusions:-

(i) The optimum temperature for the hatching of the ova was 25-30° C. and the hatching was retarded by temperatures of over 37° C.

mirac (ii) Sunlight was detrimental to hatching.

cont (iii) Oxygen was essential for the development of the miracidia.

because (iv) The miracidia died within 16 days in a urine faeces mixture.

village (v) The chemicals which killed the snails, and the cercariae, also killed the miracidia.

being Faust and Meleney⁵, in the course of their experiments, found that the upper limit of temperature for the hatching of the ova was 43° C. They also found that certain chemicals like calcium chloride (sp. g.

and the education of the people in a mode of life

1050 or over), cresyl blue, Nile blue sulphate, and potassium alum (1 percent), destroyed the miracidia in a very short time. Another interesting point, they brought out was, that the fermenting organisms present in the stools retarded the hatching of the ova, and killed the miracidia in about four days if the stools were not diluted with water. It has been known that the miracidia are killed rapidly in acid media. Miyagawa and Loos have shown that the miracidia die in dilute hydrochloric acid (.05 %).

Out of these factors, the one that has been most useful in its practical application, is the storage of faeces for a period of three weeks in countries like China, where human excreta is used as a fertilizer.

The ideal to be attained would be the institution of well-regulated sewage disposal systems in the endemic areas, to ensure the destruction of the miracidia, before the sewage is allowed to come in contact with the intermediate hosts. This, however, is not an easy matter in most of the endemic areas, because of the tremendous expenditure involved, and the scattered nature of the population in most small villages.

Another useful method, which is at present being attempted in Egypt, consists in the erection of latrines in the villages, and inducing the people to use them. Here again, the expenditure involved may prove to be a serious drawback in some localities, and the education of the people in a mode of life,

contrary to their customs and traditions is no easy matter. It has been a custom in Egypt, since times immemorial, for the people to ease themselves along the banks of their water ways, and to use the water for their ablutions subsequently. The aid of the religious heads may be sought to impress upon the people, the dangers associated with these practices.

The measure of success to be expected from the employment of these methods, is not very great, and it may take prolonged efforts on the part of the state, to educate the people with regard to these points; but nevertheless they cannot be neglected.

Once the population of the heavily infected areas is made conscious of its responsibility, the control of this disease may become a comparatively simple matter.

(3) Destruction of the intermediate hosts:- This method of control of schistosomiasis, has been tried extensively in Japan, and lately in Egypt. Satisfactory results can only be obtained if the destruction is thorough, otherwise the few snails that may be left over, would start breeding again as soon as the conditions become favourable for their growth and development.

One advantage of this method is that, in addition to controlling schistosomiasis, the spread of certain other trematode worms, which also use these snails as intermediate hosts, is checked to some extent.

Most of the methods described for the destruction of snails have their limitations, and the method of choice in any particular locality, has to be selected according to the prevailing conditions. The various methods that have been tried may be classified as follows:-

(i) Dessication of the water ways.

(ii) By the employment of chemical and other poisons.

(iii) By the employment of our knowledge of the bionomics, and the habits of the snails.

(i) Dessication of the water ways:- Leiper (1915-18)⁶ found that the snails found in the dry beds of canals, failed to revive when placed in water. He recommended the utilisation of periodical drying of the territory canals as a means of combating schistosomiasis in Egypt.

The results of carefully controlled experiments in the Public Health Laboratories, Cairo⁷, in 1924 confirmed this. It was found that Planorbis boissyi, Bullinus dybowskyi, and Bullinus contortus snails died within 3-5 days if placed in petri dishes lined with filter papers, in the shade at ordinary temperatures.

It would seem from the above, that in the irrigated parts of Egypt, where during the summer months (April-August), the water supply to each canal was periodically closed (6 days flow being followed by a fortnight's cessation), all snails should have been destroyed. But it was found that some small puddles persisted in the beds of these canals, and

tion, which protects them from the effects of

some of the snails survived in these providing a 'carry over' till the water supply was restored again. Leiper suggested that this could be avoided by either improving the alignment of the canals, or by using chemicals e.g., ammonium sulphate to kill the snails in these puddles.

This method of attack on the snail host has to be augmented by the constant removal of rushes, water weeds, grass, and any other kind of floating vegetation, which may otherwise provide shelter to the snails during the dry periods. Wire-gauze filters have been recommended to prevent the snail-laden weeds from finding their way into the canals.

It has further to be remembered that all snails are not destroyed by dessication. Blacklock and Thompson⁸ have shown that Physopsis globosa snails can survive dessication for 14 days in mud in the shade. They state "Merely cutting off or diverting the water for a few days in infected areas, will not ensure the death of all, or probably even many of these snails". Cawston⁹ has also commented on the fact that snails can stand drying for a long time. Recently Barlow¹⁰ has stated that snails in Egypt can remain alive for months of drying, by secreting some slimy material, and forming an epiphragm. The snails belonging to the genus *Onchomelania* are operculated, and can consequently resist drying and dessication for a long time (three months according to Cort)¹¹.

The ova of the snails, which are usually laid on stones or weeds, are bound down by a sticky secretion, which protects them from the effects of

dessication.

Calcium cyanamid (CaCN_2) has also got the advantage of being a useful fertilizer, and it appears to be even more potent than lime in killing snails (A 0.1 % solution killed all snails within 3 days), but it is comparatively more expensive, and therefore has not been used very extensively.

This method, evidently can have very limited application, being practicable only in artificially irrigated areas. Even in these areas, though it may not be expected to completely exterminate the intermediate hosts, it may be valuable in producing e.g., Calcium phosphate $\text{Ca}_3(\text{PO}_4)_2$, and ammonium sulphate $(\text{NH}_4)_2\text{SO}_4$.

(ii) By the employment of chemical and other poisons:-

and Copper sulphate (CuSO_4).

This method has been tried extensively in Japan. The most important point in the selection of a suitable substance is that it should be lethal to the snails in high dilutions, but harmless to human beings and plants, or better still which

Extensive experiments were conducted in the Public Health Laboratories, Cairo, to estimate the value of copper sulphate in snail destruction, using

It was found that unslaked lime (CaO) was useful in destroying snails (Fujinami and Sueyasu¹² and *Physa subcapa* snails, and the following conclusions were arrived at:- snails within 5 days), and it was also a good

1. *Bullinus* snails were found to be more susceptible to the action of copper sulphate than with a considerable amount of success. In irrigation ditches, it was used as a 1 % solution, and was

2. Copper sulphate was found to be more effective when dissolved in distilled water as compared with tap water. It was least effective in river or prevent injury to the crops.

Calcium cyanamid (CaN.CN) has also got the advantage of being a useful fertilizer, and it appears to be even more potent than lime in killing snails (A.O.1 % solution killed all snails within 3 days), but it is comparatively more expensive, and therefore has not been used very extensively.

Most of the other chemicals that have been tried, fall under two headings:- (a) Useful fertilizers, but not very efficient in killing the snails e.g., Calcium phosphate $\text{Ca}_3(\text{PO}_4)_2$, and ammonium sulphate $(\text{NH}_4)_2\text{SO}_4$. (b) Effective in killing snails but harmful to crops e.g., Chlorinated lime (CaClOCl), and Copper sulphate (CuSO_4).

Out of these, unslaked lime is the most suitable one for use in agricultural areas, where snails are to be destroyed without injuring the plants, because of its low price.

Extensive experiments were conducted in the Public Health Laboratories, Cairo¹³, to estimate the value of copper sulphate in snail destruction, using P. boissyi, B. dybowski, B. contortus, Physa acuta, and Physa subopaca snails, and the following conclusions were arrived at:-

1. Bullinus snails were found to be more susceptible to the action of copper sulphate as compared with Planorbis.

2. Copper sulphate was found to be more effective when dissolved in distilled water as compared with tap water. It was least effective in river or

inhabitants were infected with schistosomiasis pond water; the greatest dilution with which it was possible to kill the planorbis, and Bullinus snails the main stream, for four days and nights, killed all being 1 in 300,000 to 1 in 200,000.

3. It was also found that the addition of algae or soil to the water, reduced the potency of the drug to a certain extent, and therefore the lowest effective concentration of the drug, in canals and ditches was estimated to be 1 in 3-200,000.

4. As copper sulphate is soon eliminated from water under natural conditions, partly by being precipitated, and partly by being fixed by the algae etc., it is not harmful to human beings in these dilutions.

5. It was found that copper sulphate employed in the strength of 10 parts per million, had no deleterious effect on cotton, maize, or wheat, in their germination stages; nor did the grown plants of cotton, maize, sugarcane, rice etc., suffer from any harmful effects due to irrigation with the same solution.

Colloidal copper was found to be even more effective; it killed all snails in a concentration of 1 in 400,000 in crude Nile water. But this is not likely to replace copper sulphate, because it is too expensive, and not being available in a concentrated form, has to be carried about in bulk.

¹⁴ Khalil has described a successful attempt in destroying all snails by using copper sulphate in a village in the Oasis Dakhla, where 63.5 % of the

inhabitants were infected with schistosomiasis haematobium. Copper sulphate, added continuously to the main stream, for four days and nights, killed all snails, and no snails were seen in that stream 6 months later.

These results are certainly very encouraging, and the use of copper sulphate would appear to be the method of choice in localities where the fertility of the land is not the first consideration. Otherwise unslaked lime is best.

Fujinami and Sueyasu investigated the possibility of using heat in killing snails. They found that all snails died instantaneously in hot water at a temperature of 60° C. This has no practical value, because even boiling water becomes quickly cooled when sprinkled on the soil. Live steam was found to be more useful if expelled through a hose, under a piece of heavy canvas; 90 % of the snails within the area being killed within a short time. This method has been tried extensively in the Katayama district of Japan, but had to be given up because it was found to be too expensive and cumbersome.

Sea water also has been found to kill snails within a short time. Faust and Meleney¹⁵, working with Japanese Katayama snails, found that a strength of equal parts of sea water and tap water was lethal to the snails within 24 hours. This method may be employed with advantage in endemic areas along the sea shore, but here again the expenditure involved is a drawback.

Several other methods have been advocated to attack the molluscan hosts of these parasites; though these cannot be relied upon to rid a given area completely of the snails, they may be useful in reducing their numbers, and may be applied in addition to the methods already described.

It has been said that birds can play a part in reducing the number of snails; Cawston¹⁶ is of opinion that the domesticated duck is very useful in controlling the number of snails in a pond. Though, this method can hardly be expected to irradicate the intermediate hosts in any place, yet the ease with which it can be applied, should certainly make it worth the trial.

Certain plants have been described to be naturally poisonous to snails. Cawston¹⁷ recommends the cultivation of the plant Tophorana macropoda, which he had found to be toxic to the *Physopsis* snails. Archibald¹⁸ has found that the fruit of the tree Ballanites aegyptica is poisonous to snails, miracidia, cercariae, tadpoles, fish etc., and recommends the following method for its use:-

35 of the date like berries obtained from this tree should be soaked in $4\frac{1}{2}$ gallons of water over night, crushed, and allowed to stand for another 24 hours. This, if added to a cubic foot of infected water, can kill the schistosome larvae within 1 hour, and the snails within 12 hours.

Cawston¹⁹ has recently advocated another method, which may be useful in certain ponds and tanks. He

found that the common water hyacinth Eichhornia crassipes, if introduced into a pond, can outgrow and oust other weeds and plants, which the snails feed on, and thereby produce a material reduction in the number of the snails. In a later communication, the same author has recommended the control of rushes and water lilies in the tanks and ponds in the endemic areas.

(iii) The employment of our knowledge of the bionomics, and habits of the snails:- As the knowledge with regard to the habits of these molluscs is improving, the problem of their control is becoming comparatively easier. It is always a great advantage to have some idea regarding the habits of the local species of snails, before starting a campaign against them in any particular area.

Leiper It has been found, that *Planorbis* is usually a surface feeder, and favours either slowly moving, or stagnant muddy water. It feeds on rushes and grasses growing at the margins of the water. Its breeding season is most probably during late spring (April and May), the eggs being often deposited on the shell of another member of the same species.

media, *Bullinus* and *Physopsis* snails are very similar in their habits. They prefer clear water as found in tanks, and more swiftly flowing water ways. They are usually found attached to stones, posts etc., at some considerable depth below the surface. The eggs are usually found deposited on stones at the bottom of the water.

According to Kan and Yao²⁰ the *Onchomelania* snails are amphibian in nature, being found in water, as well as in moist soil, under grass or stone pieces. They conjugate in March and April, and oviposit in May. They live on putrified matter, having special preference for human faeces.

The snails usually take about three months to attain maturity.

It would obviously be a great advantage to keep the important points regarding the habits, and bionomics of the local snails, in mind, when planing any particular method of attack against them. For instance, the domesticated duck would be more useful in dealing with the surface snails e.g., *Planorbis*.

As most of the snails are distributed, either along the surface, or at the bottom of the water, Leiper has suggested that the intake pipes for storage tanks etc., should be taken from the middle to minimise the inclusion of snails and cercariae.

Atkins^{21,22} has shown that the distribution of snails is affected by the hydrogen ion concentration of the soil, and water, which also affects the liberated cercariae. They thrive best in neutral or alkaline media, pH 7-8 being most suitable. He suggests that the alkalies (Sodium and potassium carbonates) which can be easily obtained by burning grass, and other vegetation should be used to change the reaction of the water in small ponds and tanks.

The comparative measure of success in prophylaxis, that can be expected from snail destruction,

also depends on the size of the endemic area, and the distribution of the snails. Best results can be expected in a country like Japan, where the endemic areas, as well as the specific snails, are restricted to small areas of a few square miles each.

In countries like China, and the Sudan on the other hand, where the endemic areas are scattered over thousands of square miles, it may be difficult to deal with the snail hosts, and resource should be had to the more thorough application of the other methods, e.g. the control of the dejecta, and the water supplies etc.

(4) Attack on the cercariae, and prevention of infection of the adult host:- Most of the chemical and other substances used for snail destruction, are lethal to the cercariae also, and consequently where those are being applied, the cercariae will also succumb.

The object to be attained in connection with this method is to prevent infected water from coming in contact with human beings, until such time when all cercariae have been killed.

Shallow ponds and ditches containing infected water should be drained and dried up. In larger tanks where this is not possible, the cercariae may be attacked by using some chemical e.g., copper sulphate. This can only be useful if all infected snails in the particular tank are also dealt with.

Where the destruction of the cercariae, and the snails is not practicable, Clunner²³ recommends that all

infected tanks should be marked out as dangerous; but it is doubtful if it would prevent the ignorant people, especially the children, from exposing themselves to infection.

Apart from dealing with collections of infected water around inhabited areas, the most important method for preventing infection amongst human beings is to provide a non-infective water supply.

Leiper has shown that the Jewell system of filtration, as used in the ordinary municipal filter bed, is ineffective in stopping the cercariae; he found that the cercariae were active after penetrating 30 inches of sand, which they accomplished in 5 hours. He said that the efficiency of such mechanical systems depends solely on the delay interposed "between the discharging mollusc and the consumer".

He also found that the shallow sand filters, were equally inadequate; cercariae were able to pass through 4 inches of desert sand in 15 minutes.

If water could be stored for 48 hours, before being issued out, all cercariae would be killed.

Great care has to be taken to exclude the infected snails from the storage tanks in the employment of this method. This can be easily achieved by screening the inlet pipes with wire-gauze of about 16 meshes to the linear inch. The immature snails that may pass through, are not dangerous, because they cannot be infected.

Chlorine, in the strength usually employed as a Bactericide is harmless to the cercariae. It

can kill the cercariae in higher concentrations, which makes the water unpalatable. Leiper recommended that it should be used in the strength of 20 parts per million of bleaching powder, and the water subsequently dechlorinated.

Griffith Jones, Atkinson, and Ali Hassan,²⁴ compared the relative killing powers of chlorine and chloramine on schistosome cercariae, and came to the following conclusions:-

1. Both S. haematobium, and S. mansoni cercariae are susceptible to the action of chlorine and chloramine.

2. Chlorine in the strength of 1 in 1,000,000 killed all cercariae in $2\frac{1}{2}$ -3 hours. They recommend that the water should be stored for 3-4 hours when treated with chlorine.

3. Chloramine, when prepared in the apparatus supplied by Messrs United Water Softeners Limited, according to the printed instructions supplied, was very unstable. But if prepared by the modified 'water cart' method (vide infra), it gave better results than chlorine. In a strength of 1 in 1,000,000, it killed all cercariae in one hour. The method recommended by the authors, for the preparation of chlorine is as follows:-

"To a jar containing about 20 litres of tap water .78 gms. of ammonium chloride (equivalent to 10 parts per million NH_3) in 25 litres was dissolved, and 250 c.cm. of chlorine water, prepared in the apparatus, and adjusted to 3,000 parts per million,

was added by pouring down a rapid stream of tap water into the jar, and shutting off the tap when the level reached the 25 litre mark. Thorough mixing was ensured by further stirring. This contained 20 parts in 1,000,000 of chloramine."

It was found that a considerable proportion of chloramine was absorbed, when mixed with crude Nile water. For practical use they recommend, that chlorine should be used in 3 parts per million strength, followed by subsequent dechlorination.

For washing and bathing purposes, the water can be rendered harmless by using other chemical agents e.g., ammonium sulphate, cresol 1 in 1,000, creolin, lysol etc.

For drinking water, boiling is by far the best method, all cercariae being killed instantaneously at a temperature of 50° C. Water from wells is considered safer than canal or tank water, because no snails are found in the wells. Where boiling is not possible, drinking water may be quickly sterilised by the addition of sodium bisulphate (1 tablet of 16 gr. to the pint, which equals a dilution of 1 in 567). This kills all cercariae, and is harmless to human beings.

²⁵Bettencourt tried the effect of soapy water on cercariae, and found that under natural conditions in river or canal water it soon becomes innocuous due to precipitation by the salts. He found that washer-women in Tavira, Portugal, became infected in spite

ments, although they were obtained from Planorbis

of the soap in the water. these results are doubtful.

(b) Personal prophylaxis:- chlorination are

This is essentially a matter for propaganda, and education of the people in the endemic areas, and applies especially to people who are visiting these areas. Men who are detailed to draw water from the

canals. It is very important to prevent infection amongst troops visiting the endemic areas, because in addition to the ill health and the lack of efficiency that may result, there is a danger of the disease being spread to other areas where it is so far unknown. This however, depends on the presence of the specific intermediate hosts in these areas. ere, reaching well

above Strict discipline regarding water, with some illustrated lectures to explain the nature of the disease, and the risk run by those exposing themselves to infected water, should minimise the danger. The various methods that have been recommended for killing the cercariae in drinking water, as well as the water for washing and bathing purposes, have already been discussed.

The problem of prophylaxis in the Far East:-
If the 'water cart' method of disinfecting

In these areas the control of the disease is water is in use, the strength of chlorine should be even more difficult, because of the existence of increased to 3-4 parts per million, and the water 'reservoir' hosts amongst the animals. The universal kept for about four hours, and dechlorinated before use of human excreta for fertilizing purposes in being issued out. Blackmore found that 1 part per Japan and China further complicates the problem. million, of chlorine killed all cercariae in half an hour. In Japan the disease is being successfully controlled by combining the methods directed against experiments has not been proved by the animal experiments, with the destruction of the infected the snails. Although they were obtained from Planorbis

boissyi snails, so perhaps these results are doubtful. areas Where boiling, storage, or chlorination are not possible, drinking water may be quickly sterilised by dissolving 2 tablets of sodium bisulphate in a quart water bottle.

Men who are detailed to draw water from the canals, and all others who are likely to come in contact with infected water, should be specially protected.

Sportsmen visiting infected areas should be warned, where possible to take adequate precautions. Those engaged in snipe, or duck shooting should provide themselves with rubber waders, reaching well above the umbilicus. Fishing also is attended with some risk, and fishermen should be advised to protect themselves by using proper waders, and rubber gloves.

As the snails and the cercariae are unable to survive in sea water, the salt water swamps are quite safe from infection.

The disease is so far restricted to certain villages

The problem of prophylaxis in the Far East:- (the infection usually being very intense in these).

In these areas the control of the disease is but as communications improve, and travel increases, even more difficult, because of the existence of it is bound to spread more diffusely.

'reservoir' hosts amongst the animals. The universal use of human excreta for fertilizing purposes in the ignorance and superstition amongst the peasantry Japan and China further complicates the problem.

In Japan the disease is being successfully controlled by combining the methods directed against the snails, with the destruction of the infected containers, known as 'kange'; fresh excreta being

animals. In that country, the size of the endemic areas being small (usually a few square miles only), makes it possible to deal with the problem more thoroughly.

Miyagawa²⁷ described that the lampyrid larva of the glow-worms (*Luciola* p.) is a natural enemy of the snail host of *S. japonicum*, and kills all the snails when the two are confined together. This observation appears to be of academical interest only, and does not seem to have been applied in practice.

In China, the disease has been reported to extend over a vast territory, the Shaokan-Tsaoshih area in Hupeh province, for instance, which is the smallest endemic region of the Yangtze basin, has an area of about 600 square miles.

According to Faust and Meleney, the area of the rice growing country in China, in which both the disease and the intermediate host are present, is estimated to be at least 25,000 square miles. Due to the small amount of travelling done by the farmers, the disease is so far restricted to certain villages (the infection usually being very intense in these), but as communications improve, and travel increases, it is bound to spread more diffusely.

The lack of proper sanitary arrangements, and the ignorance and superstition amongst the peasantry makes the problem much more complex in China, as compared with Japan. Human excreta is stored in huge earthenware containers, known as 'kangs'; fresh excreta being

(1) The control of cercarial dermatitis. This added from day to day. When the fertilizer is comprises four main subsidiary measures: required for the fields, these kangas containing a mixture of ripened, and fresh excreta are emptied. (i) Adequate storage of the kangas to ensure the destruction of all cercariae. To be on the safe side, faeces should be stored for a period of at least three weeks, before being applied to the fields. Faust and Maloney have suggested, that the period of storage could be reduced, if some suitable chemical was found, which could kill the cercariae in these kangas, and had fertilizing properties also. Fresh faeces are considered to be better fertilizers, than faeces which have ripened. The buckets, and ladles, used in emptying the kangas are usually washed in the canals.

The farmers wade freely (with bare arms and legs) in water in the nursery beds (where rice is first sown), and the flooded rice fields; both of which usually contain cercariae of S. japonicum in the endemic areas. (ii) The avoidance of promiscuous defaecation: This is even more difficult to control than (i), because it would need extensive propaganda. Fortunately,

In these areas, transport is mainly by water, canals being practically the only route of travel in the flat rice country. The boatmen and their families find its way into the kangas. Attempts should also be made to prevent the boatmen from fouling the canals; for all necessary purposes in the house. Men and children wade freely in this canal water. These boatmen may play an important part in the dissemination of the disease, because they travel to the various parts of the country. (iii) The habit of washing commodes, buckets, ladles, etc. (used for transporting excreta) in the canals should be stopped, unless they have been first sterilised in boiling water, or lime. This again, may be very difficult to enforce.

Having discussed the main points in connection with the propagation, and spread of the disease in far as possible. Kan and Yao have shown that in Chekiang, the principal prophylactic methods suitable for that country will now be described. (iv) Reservoir hosts should be eliminated as far as possible. Kan and Yao have shown that in Chekiang, the principal prophylactic methods suitable for that country will now be described. (v) Reservoir hosts should be eliminated as far as possible. Kan and Yao have shown that in Chekiang, the principal prophylactic methods suitable for that country will now be described.

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(1) The control of contaminated faeces:- This comprises four main sanitary measures:-

(i) Adequate storage of the faeces to ensure the destruction of all miracidia. To be on the safe side, faeces should be stored for a period of at least three weeks, before being applied to the fields. Faust and Meleney have suggested, that the period of storage could be reduced, if some suitable chemical was found, which could kill the miracidia in these kangas, and had fertilizing properties also.

(ii) The avoidance of promiscuous defaecation:- This is even more difficult to control than (i), because it would need extensive propaganda. Fortunately, night soil is considered a valuable fertilizer in China, therefore it is usually seen that most of it finds its way into the kangas. Attempt should also be made to prevent the boatmen from fouling the canals; in this case the inducement of getting some money for their excreta, as is quite common in parts of the Chekiang province, may be much more effective, than all the propaganda, and lecturing.

(iii) The habit of washing commodes, buckets, ladles, etc. (used for transporting excreta) in the canals should be stopped, unless they have been first sterilised in boiling water, or lime. This again, may be very difficult to enforce.

(iv) Reservoir hosts should be eliminated as far as possible. Kan and Yao have shown that in Cheh-huai-pan, Kaihua, Chekiang, cattle and dogs are most commonly infected. The contact of these animals with

infected water, should be avoided as far as possible. Those found infected, are best destroyed.

(2) Avoidance of contact with infected water:-

The small terminal canal, and the irrigation ditch, are potent sources of infection, but the most dangerous is the rice nursery bed, where fresh faeces are applied. Some method of protection of the feet, and hands of the farmers, while working in these should be employed.

The permanent rice fields are comparatively less dangerous. It has been recommended that the farmers should use a thick coating of some heavy oil or grease on their arms and legs, but the value of these in preventing infection is doubtful.

Browne has recorded a case, where an officer got infected while snipe shooting in infected water, in spite of the fact he had smeared his legs with carbolised vaseline, and scrubbed himself thoroughly on getting back.

(3) The treatment of infected cases, though it may not be directly useful as a general prophylactic measure, as it is in Egypt, should be carried out extensively in the infected areas.

Faust and Meleney have said "Successful treatment of the disease would also be a potent factor in the education of the people by gaining their confidence in the advice given, and co-operation in the carrying out of preventive measures."

(4) The destruction of the intermediate hosts:-

In China the snails are distributed over vast areas,

The problem of prophylaxis in India:-
and as already stated, the *Onchomelania* snails are able to live in water, as well as on moist soil. This makes the problem of snail destruction very difficult.

It may be of advantage to reduce their numbers, in the small canals, and the nursery beds, by using lime, or some other chemical fertilizer which is lethal to snails in high dilutions.

Kan and Yao have recommended that in winter the grass should be burnt, and the ditches and the rice fields should be skimmed, and sprayed with lime water. In summer, unslaked lime should be used in the irrigation ditches, and the nursery beds. The country is so vast, and the nature of the country, the habits, religions, and customs of the people vary so greatly, that the problem for any given area will have to be solved separately.

Northern India, especially the Punjab, provides an illustration of an area, artificially irrigated, where the irrigation is under control. The Central, and the United Provinces are illustrations of areas where irrigation can not be strictly controlled. In Rajputana, the main source of water supply is from wells and lakes.

Apart from the water supply of the various parts of the country, the most important point would be to educate the rural population, and teach them the simple hygienic points, which would help in checking the spread of schistosomiasis as well as several other infectious diseases. Fortunately, this is receiving a lot of attention from the Government at the present

The problem of prophylaxis in India:-

As upto the present moment, schistosomiasis does not appear to be prevalent in India, the problem should be much easier as compared with countries, where this disease has been endemic for hundreds of years. It need hardly be emphasised, that in this country, the most important point is to prevent the disease from taking a hold, by aborting any threatened outbreak by active measures at the earliest possible moment.

In the case of an outbreak, the exact prophylactic measures will depend on the part of the country involved. The country is so vast, and the nature of the country, the habits, religions, and customs of the people vary so greatly, that the problem for any given area will have to be solved separately.

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time, and though for obvious reasons, the results of these rural uplift schemes are going to be slow in practice, there is no doubt that it must prove most useful in the long run.

The exact methods suitable for the principal areas, may be summarised as follows:-

1. The Bombay presidency is an example of an area, where the main source of water supply is from lakes, the water level in which depends on the rains. These lakes mostly contain a variety of snails, and in case of infection these will have to be dealt with. In these areas, treatment of the infected people, and prevention of contamination of the lakes, in addition to the provision of a cercaria-free water supply (where possible) would be indicated. Any animals that may get infected may have to be destroyed. There is a natural protection in ponds and lakes along the coast, by their being flooded with salt water during the monsoon season.

Artificially treating the various collections of water along the coast, with sea water, however, would be too expensive to be practicable.

2. The Punjab is traversed by a net work of artificial canals, which in case of infection could be best dealt with by periodical dessication. In most of the villages in this province, drinking water is obtained mainly from wells, which are free from snails. The most dangerous place around a village in this part of the country is the village pond, which fills up during the rains, and persists for the best part of the year. It is freely used for disposing of all kinds of filth, and

during the heat of the day children, as well as domestic animals wade about in it. These ponds however, are usually small enough in size to be amenable to disinfection with some reliable chemical, e.g., copper sulphate, without causing much inconvenience to the inhabitants.

3. In Rajputana, the main source of water supply is from wells. The few ponds and puddles, which form after the rains, usually dry up within a few days after the monsoons. Even most of the smaller lakes dry up during the hot season, and the few that persist can be easily dealt with.

4. The rice growing country in Bengal and Madras would present a problem not unlike China. Human excreta is not used as a fertilizer to the same extent in this country, nor do we have a parallel to the canal system of China. Unslaked lime would appear to be the ideal disinfecting agent for these areas.

Though active prophylaxis in any part of the country would depend largely on the local conditions, the most important points are the education of the rural population, and vigilance on the part of the medical profession, and the public health departments.

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Conclusion:- It may be stated in conclusion that the position with regard to the spread of the disease has improved considerably.

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efforts of the various investigators, the future is definitely hopeful, and as the sanitary and educational conditions, in the endemic areas improve schistosomiasis should slowly disappear.

In Fouadin we have a reliable and safe specific for the disease, but it falls short of being the ideal drug. It is hoped that before long a drug will be found which can be administered orally, and is cheap enough for employment on a large scale.

From the data available, and the results of the author's investigations in Bombay, it would appear that this disease most probably does not affect the human beings in this country.

It is possible that the snails found in this country, though morphologically allied to those found in some of the endemic areas, are not suitable for the development of the larvae of the schistosome worms which attack man. Until such time, when this can be proved by experimental work in various parts of the country, the possibility of the introduction, and spread of schistosomiasis can not be ignored.

In the event of the disease making its appearance in any part of the country, active prophylactic measures, on the lines laid down, will have to be employed to prevent its spread. If, on the other hand, the disease is

Conclusion:- It may be stated in conclusion that the position with regard to this wide spread disease has improved considerably during the past few years. In spite of the profound pathological changes it produces in the bodies of hyper-infected people, thanks to the efforts of the various investigators, the future is definitely hopeful, and as the sanitary and educational conditions, in the endemic areas improve schistosomiasis should slowly disappear.

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In the event of the disease making its appearance in any part of the country, active prophylactic measures, on the lines laid down, will have to be employed to prevent its spread. If, on the other hand, the disease is

once allowed to establish itself to any extent in this country, the problem of control may assume a greater magnitude than it does in countries like China and Egypt. It is therefore the duty of the State, and the medical profession in general to see that schistosomiasis does not add itself to the already long list of the public health problems of India.

Summary:-

1. A resume has been written, of our accumulated knowledge of *Schistosomiasis japonicum*, based on the works and the conclusions arrived at by many original investigators, and the important points of difference with the other two types of human schistosomiasis have been brought out.

2. Various aspects in regard to the history, the incidence, and distribution of the disease, the life history of the organisms, and the pathological effects produced on the human host have been considered.

3. An account is given of the snail hosts concerned with the development of the parasites in the various endemic areas.

4. The symptomatology, diagnosis, prognosis, and treatment of the disease have been discussed as fully as possible.

5. The results of the examination of the cercariae obtained from a large number of snails, collected from various fresh water tanks and ponds in and around Bombay have been noted. The seasonal infective index

of Indoplanorbis exustus snails with S. spindalis

has been worked out over a period of 15 months.

6. The results of the clinical and laboratory investigations, carried out in a certain number of specially selected cases in Bombay, to detect possible infection with S. japonicum have been described.

7. The problem of prophylaxis, as it affects the various endemic areas, has been discussed in detail, and the special measures which will be suitable in dealing with a possible out break in this country have been outlined.

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